

FIG. 1

|                        |     |     |     |     |     |     |     |     |     |     |     |     |     |
|------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Bovine cDNA            | 1   | 5   | 10  |     |     |     |     |     |     |     |     |     |     |
|                        | Met | His | Ser | Asp | Cys | Ile | Phe | Lys | Lys | Glu | Gln |     |     |
|                        | *   | *   | *   | *   | *   | *   | *   | *   | *   | *   | *   |     |     |
| Purified bovine Sample | Met | His | Ser | Asp | Cys | Ile | Phe | Lys | Lys | Glu | Gln |     |     |
|                        | 15  | 20  | 25  |     |     |     |     |     |     |     |     |     |     |
| Ala                    | Met | Cys | Leu | Glu | Lys | Ile | Gln | Arg | Val | Asn | Asp | Leu | Met |
|                        | *   | *   | *   | *   | *   | *   | *   | *   | *   | *   | *   | *   | *   |
| Ala                    | Met | Cys | Leu | Glu | Lys | Ile | Gln | Arg | Val | Asn | Asp | Leu | Met |
| Gly                    | Leu | Asn | Asp |     |     |     |     |     |     |     |     |     |     |
|                        | *   | *   | *   | *   |     |     |     |     |     |     |     |     |     |
| Gly                    | Leu | Asn | Asp |     |     |     |     |     |     |     |     |     |     |

FIG. 4

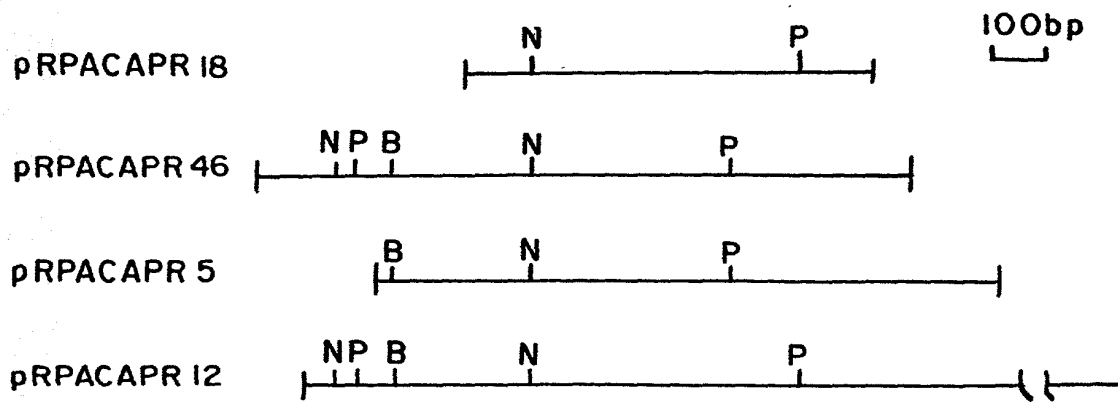


FIG. 6

|   |            |   |            |            |            |      |
|---|------------|---|------------|------------|------------|------|
| TGGCCTGCAC  | CCCACCCCCC | AGCCTGCGAA                                  | GACGGGGGGA | GGCGGTGGTC | GGTCGCCTCC | 60   |
| CTCCTGCCCC  | CGGCCTGGCT | TCGCGGTGGA                                  | GGCGGTGCCT | CTCCGGCAAG | GCAGACCAGG | 120  |
| CTGGGCGGAC  | GCGCGGCGCG | GGGCGGGCTA                                  | GGGAAGGCCG | GGGGCCTCGC | GCTCGGGCCC | 180  |
| CGGGCGGCGA  | CTGACAGCGG | CGGCGGCGGC                                  | GGCAGCGGCT | CCAAGGCGAG | CGTGGTCCCC | 240  |
| GCGTGCGCAC  | AAGCTCGCCG | CCGCGCAGGG                                  | ACCCACGGAC | ACCGGCGCCG | GGCGGACACA | 300  |
| CAGACGCGGA  | GATCGGGCTC | TACGCGCGCT                                  | ACTCAGCGCA | CGAGCTCCCC | ATCCCTGGGC | 360  |
| GGAGCGGGGC  | GCGGACTCGC | CGCTGCGCGC                                  | CCTCCCCGCG | GAGTCTGCCC | CGGGCAGACC | 420  |
| CGCAGCCCGC  | GGCCCCGCGG | CGAGGCCCT                                   | GGGTGAGCAG | CCTGTAGACA | CCTGGGGTTG | 480  |
| AGCAGTGGCG  | GCTGTGA    | ATG AGA GGC GGG CGG CAC TGG CCC GAG CCG CCT |            |            |            | 530  |
|   |            | Met Arg Gly Gly Arg His Trp Pro Glu Pro Pro |            |            |            |      |
|   | 1          |   | 5          |            | 10         |      |
|   |            |   |            |            |            |      |
| TGC AGG CTG AGA AGC GTC ATG GCC AGC ATC GCG CAG GTC TCC CTG GCT |            |   |            |            |            | 578  |
| Cys Arg Leu Arg Ser Val Met Ala Ser Ile Ala Gln Val Ser Leu Ala |            |   |            |            |            |      |
|   | 15         |   | 20         |            | 25         |      |
|   |            |   |            |            |            |      |
| GCT CTC CTC CTG CTG CCT ATG GCC ACC GCC ATG CAT TCC GAC TGC ATC |            |   |            |            |            | 626  |
| Ala Leu Leu Leu Leu Pro Met Ala Thr Ala Met His Ser Asp Cys Ile |            |   |            |            |            |      |
|   | 30         |   | 35         |            | 40         |      |
|   |            |   |            |            |            |      |
| TTC AAG AAG GAG CAA GCC ATG TGC CTG GAG AAG ATC CAG AGG GTG AAT |            |   |            |            |            | 674  |
| Phe Lys Lys Glu Gln Ala Met Cys Leu Glu Lys Ile Gln Arg Val Asn |            |   |            |            |            |      |
|   | 45         |   | 50         |            | 55         |      |
|   |            |   |            |            |            |      |
| GAC CTG ATG GGC TTG AAT GAC TCC TCC CCA GGG TGC CCT GGG ATG TGG |            |   |            |            |            | 722  |
| Asp Leu Met Gly Leu Asn Asp Ser Ser Pro Gly Cys Pro Gly Met Trp |            |   |            |            |            |      |
|   | 60         |   | 65         |            | 70         | 75   |
|   |            |   |            |            |            |      |
| GAC AAC ATC ACG TGT TGG AAG CCC GCC CAC GTG GGT GAG ATG GTC CTG |            |   |            |            |            | 770  |
| Asp Asn Ile Thr Cys Trp Lys Pro Ala His Val Gly Glu Met Val Leu |            |   |            |            |            |      |
|   |            | 80  |            | 85         |            | 90   |
|   |            |   |            |            |            |      |
| GTC AGT TGC CCT GAA CTC TTC CGA ATC TTC AAC CCA GAC CAA GTC TGG |            |   |            |            |            | 818  |
| Val Ser Cys Pro Glu Leu Phe Arg Ile Phe Asn Pro Asp Gln Val Trp |            |   |            |            |            |      |
|   |            | 95  |            | 100        |            | 105  |
|   |            |   |            |            |            |      |
| GAG ACG GAA ACC ATC GGA GAG TTC GGT TTT GCA GAC AGT AAA TCC TTG |            |   |            |            |            | 866  |
| Glu Thr Glu Thr Ile Gly Glu Phe Gly Phe Ala Asp Ser Lys Ser Leu |            |   |            |            |            |      |
|   | 110        |   | 115        |            | 120        |      |
|   |            |   |            |            |            |      |
| GAT CTC TCA GAC ATG AGG GTG GTG AGC CGG AAT TGC ACG GAG GAT GGA |            |   |            |            |            | 914  |
| Asp Leu Ser Asp Met Arg Val Val Ser Arg Asn Cys Thr Glu Asp Gly |            |   |            |            |            |      |
|   | 125        |   | 130        |            | 135        |      |
|   |            |   |            |            |            |      |
| TGG TCA GAG CCA TTC CCT CAT TAT TTC GAT GCC TGT GGG TTT GAG GAG |            |   |            |            |            | 962  |
| Trp Ser Glu Pro Phe Pro His Tyr Phe Asp Ala Cys Gly Phe Glu Glu |            |   |            |            |            |      |
|   | 140        |   | 145        |            | 150        | 155  |
|   |            |   |            |            |            |      |
| TAC GAA TCT GAG ACT GGG GAC CAG GAT TAC TAC TAC CTG TCA GTG AAG |            |   |            |            |            | 1010 |
| Tyr Glu Ser Glu Thr Gly Asp Gln Asp Tyr Tyr Tyr Leu Ser Val Lys |            |   |            |            |            |      |
|   |            | 160   |            | 165        |            | 170  |

FIG.2A

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |      |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| GCC | CTG | TAC | ACA | GTT | GGC | TAC | AGC | ACG | TCC | CTC | GTC | ACC | CTC | ACC | ACT | 1058 |
| Ala | Leu | Tyr | Thr | Val | Gly | Tyr | Ser | Thr | Ser | Leu | Val | Thr | Leu | Thr | Thr |      |
|     |     |     | 175 |     |     |     |     | 180 |     |     |     |     | 185 |     |     |      |
| GCC | ATG | GTC | ATC | CTG | TGT | CGT | TTC | CGG | AAG | CTG | CAC | TGC | ACC | CGC | AAC | 1106 |
| Ala | Met | Val | Ile | Leu | Cys | Arg | Phe | Arg | Lys | Leu | His | Cys | Thr | Arg | Asn |      |
|     |     | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     |     |     |      |
| TTC | ATC | CAC | ATG | AAC | CTC | TTC | GTG | TCG | TTT | ATG | CTG | AGG | GCC | ATC | TCC | 1154 |
| Phe | Ile | His | Met | Asn | Leu | Phe | Val | Ser | Phe | Met | Leu | Arg | Ala | Ile | Ser |      |
|     | 205 |     |     |     |     | 210 |     |     |     |     | 215 |     |     |     |     |      |
| GTC | TTC | ATC | AAA | GAC | TGG | ATC | CTC | TAT | GCT | GAG | CAG | GAC | AGC | AAT | CAC | 1202 |
| Val | Phe | Ile | Lys | Asp | Trp | Ile | Leu | Tyr | Ala | Glu | Gln | Asp | Ser | Asn | His |      |
|     | 220 |     |     |     | 225 |     |     |     |     | 230 |     |     |     |     | 235 |      |
| TGC | TTT | GTC | TCC | ACT | GTG | GAA | TGC | AAG | GCT | GTG | ATG | GTT | TTC | TTC | CAC | 1250 |
| Cys | Phe | Val | Ser | Thr | Val | Glu | Cys | Lys | Ala | Val | Met | Val | Phe | Phe | His |      |
|     |     |     |     | 240 |     |     |     |     | 245 |     |     |     |     | 250 |     |      |
| TAC | TGT | GTT | GTA | TCC | AAC | TAC | TTC | TGG | CTG | TTC | ATC | GAG | GGC | CTG | TAT | 1298 |
| Tyr | Cys | Val | Val | Ser | Asn | Tyr | Phe | Trp | Leu | Phe | Ile | Glu | Gly | Leu | Tyr |      |
|     |     |     | 255 |     |     |     |     | 260 |     |     |     |     | 265 |     |     |      |
| CTC | TTC | ACC | CTG | CTG | GTG | GAG | ACC | TTC | TTC | CCC | GAG | AGG | AGA | TAT | TTC | 1346 |
| Leu | Phe | Thr | Leu | Leu | Val | Glu | Thr | Phe | Phe | Pro | Glu | Arg | Arg | Tyr | Phe |      |
|     |     | 270 |     |     |     |     | 275 |     |     |     |     | 280 |     |     |     |      |
| TAC | TGG | TAC | ATC | ATC | ATT | GGC | TGG | GGG | ACA | CCA | ACT | GTG | TGT | GTG | TCT | 1394 |
| Tyr | Trp | Tyr | Ile | Ile | Ile | Gly | Trp | Gly | Thr | Pro | Thr | Val | Cys | Val | Ser |      |
|     | 285 |     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |     |      |
| GTG | TGG | GCT | ATG | CTG | AGG | CTC | TAC | TTC | GAT | GAC | ACA | GGC | TGC | TGG | GAT | 1442 |
| Val | Trp | Ala | Met | Leu | Arg | Leu | Tyr | Phe | Asp | Asp | Thr | Gly | Cys | Trp | Asp |      |
|     | 300 |     |     |     | 305 |     |     | Δ   |     | 310 |     |     |     |     | 315 |      |
| ATG | AAT | GAC | AAC | ACG | GCT | CTG | TGG | TGG | GTG | ATC | AAA | GGC | CCT | GTA | GTT | 1490 |
| Met | Asn | Asp | Asn | Thr | Ala | Leu | Trp | Trp | Val | Ile | Lys | Gly | Pro | Val | Val |      |
|     |     |     |     | 320 |     |     |     |     | 325 |     |     |     |     | 330 |     |      |
| GGC | TCC | ATA | ATG | GTT | AAT | TTT | GTG | CTC | TTC | ATC | GGC | ATC | ATT | GTC | ATC | 1538 |
| Gly | Ser | Ile | Met | Val | Asn | Phe | Val | Leu | Phe | Ile | Gly | Ile | Ile | Val | Ile |      |
|     |     |     | 335 |     |     |     |     | 340 |     |     |     |     | 345 |     |     |      |
| CTT | GTG | CAG | AAA | CTT | CAG | TCT | CCA | GAC | ATG | GGA | GGC | AAC | GAG | TCC | AGC | 1586 |
| Leu | Val | Gln | Lys | Leu | Gln | Ser | Pro | Asp | Met | Gly | Gly | Asn | Glu | Ser | Ser |      |
|     |     | 350 |     |     |     |     | 355 |     |     |     |     | 360 |     |     |     |      |
| ATC | TAC | TTC | AGC | TGC | GTG | CAG | AAA | TGC | TAC | TGC | AAG | CCA | CAG | CGG | GCT | 1634 |
| Ile | Tyr | Phe | Ser | Cys | Val | Gln | Lys | Cys | Tyr | Cys | Lys | Pro | Gln | Arg | Ala |      |
|     | 365 |     |     |     |     | 370 |     |     |     |     | 375 |     |     |     |     |      |
| CAG | CAG | CAC | TCT | TGC | AAG | ATG | TCA | GAA | CTG | TCC | ACC | ATT | ACT | CTA | CGG | 1682 |
| Gln | Gln | His | Ser | Cys | Lys | Met | Ser | Glu | Leu | Ser | Thr | Ile | Thr | Leu | Arg |      |

FIG. 2B

| 380  | 385                                 | 390                 | 395         |      |
|--|-------------------------------------|---------------------|-------------|------|
| CTC GCC AGG TCC ACC TTG CTG CTC ATC CCA CTC TTT GGA ATC CAC TAC    |                                     |                     |             | 1730 |
| Leu Ala Arg Ser Thr  | Leu Leu Leu Ile                     | Pro Leu Phe Gly     | Ile His Tyr |      |
| 400  | 405                                 | 410                 |             |      |
| ACT GTC TTT GCT TTC TCC CCG GAG AAC GTC AGC AAG AGG GAG AGA CTG    |                                     |                     |             | 1778 |
| Thr Val Phe  | Ala Phe Ser Pro Glu Asn             | Val Ser Lys Arg     | Glu Arg Leu |      |
| 415  | 420                                 | 425                 |             |      |
| GTG TTT GAG CTG GGT CTG GGC TCC TTC CAG GGC TTT GTG GTG GCT GTT    |                                     |                     |             | 1826 |
| Val Phe  | Glu Leu Gly Leu Gly Ser Phe Gln Gly | Phe Val Val Ala Val |             |      |
| 430  | 435                                 | 440                 |             |      |
| CTC TAT TGC TTT CTG AAT GGA GAG GTG CAG GCG GAG ATC AAG AGG AAG    |                                     |                     |             | 1874 |
| Leu Tyr Cys Phe Leu Asn Gly Glu Val Gln Ala Glu Ile Lys Arg Lys    |                                     |                     |             |      |
| 445  | 450                                 | 455                 |             |      |
| TGG CGG AGC TGG AAG GTG AAC CGC TAC TTC ACC ATG GAC TTC AAG CAC    |                                     |                     |             | 1922 |
| Trp Arg Ser Trp Lys Val Asn Arg Tyr Phe Thr Met Asp Phe Lys His    |                                     |                     |             |      |
| 460  | 465                                 | 470                 | 475         |      |
| CGG CAC CCA TCC CTG GCC AGC AGC GGG GTG AAC GGG GGC ACC CAG CTC    |                                     |                     |             | 1970 |
| Arg His Pro Ser Leu Ala Ser Ser Gly Val Asn Gly Gly Thr Gln Leu    |                                     |                     |             |      |
| 480  | 485                                 | 490                 |             |      |
| TCC ATC CTG AGC AAG AGC AGC TCC CAG ATC CGC ATG TCT GGG CTT CCG    |                                     |                     |             | 2018 |
| Ser Ile Leu Ser Lys Ser Ser Ser Gln Ile Arg Met Ser Gly Leu Pro    |                                     |                     |             |      |
| 495  | 500                                 | 505                 |             |      |
| GCC GAC AAC CTG GCC ACC TGAGCCCACC CTGCCCCCTC CTCTCCTCTG TACGCAGGC |                                     |                     |             | 2075 |
| Ala Asp Asn Leu Ala Thr  |                                     |                     |             |      |
| 510  |                                     |                     |             |      |
| TGGGGCTGTG GTGGGGCGCC GGCCACGCA TGTTGTGCCT CTTCTCGCCT TCGGGCAGGC   |                                     |                     |             | 2135 |
| CCCGGGCTGG GCGCCTGGCC CCCGAGGTTG GAGAAGGATG CGGGACAGGC AGCTGTTTAG  |                                     |                     |             | 2195 |
| CCTTCCTGTT TTGGCGCTGG CCCAACCACC GTGGGTCCCT GGGCCTGCAC CCAGACATGT  |                                     |                     |             | 2255 |
| AATACTCCTT AATTGGGAAG TCATCCATTC TTTCCCTTTC CCAAGTCCTT GCTTATTAAG  |                                     |                     |             | 2315 |
| AGGTTCAAGT CACCTACCCA ATTCAGAAGC TTAAGTAACC ACTAACCACC GTGACTGCGT  |                                     |                     |             | 2375 |
| GGGAGGCCTC CCATGGGCTG AGCTACTGAC TTGGCTTTGG GGGCCTTGGG CTGGGGCCCT  |                                     |                     |             | 2435 |
| CCTTAAAGCC CCCCCTGAAA TTGTCGGACC TCAAAGTGTG ACTCCTTTGA GTCTACTCGC  |                                     |                     |             | 2495 |
| CACCCCCGTG GCCCTTTGCA GCCCTGGTCC AGTCACCGAG GTTACTGGAA GTCCAGCTTG  |                                     |                     |             | 2555 |
| GATGGCCAGA CAGCTTTTGG GCACAGGCAG ACCCATGCTC ACCCAACATT TTAGTGTCCA  |                                     |                     |             | 2615 |
| GGTGCCAGG TGCCAGGTG CCCAGCTCCT GGGCATCAGA CAGTGGGAAA GCTCCAGGGA    |                                     |                     |             | 2675 |
| TCTACCATTC AGAGACTTCA GTTTGGATGT AGGGCTAAGG CCAGAGAAAA GTTCTGGAGC  |                                     |                     |             | 2735 |
| TTTTCATTTG GCCCAAGAAA AAAGTGCCAA GATCCAGAAA AGTGGATCTG AGTGGAAATT  |                                     |                     |             | 2795 |
| AGATGCAAAG AGCTTGGAG   |                                     |                     |             | 2814 |

FIG. 2C

|   |            |   |            |            |            |         |
|---|------------|---|------------|------------|------------|---------|
| TGGCCTGCAC  | CCCACCCCCC | AGCCTGCGAA                                  | GACGGGGGGA | GGCGGTGGTC | GGTCGCCTCC | 60      |
| CTCCTGCCCC  | CGGCCTGGCT | TCGCGGTGGA                                  | GGCGGTGCCT | CTCCGGCAAG | GCAGACCAGG | 120     |
| CTGGGCGGAC  | GCGCGGCGCG | GGGCGGGCTA                                  | GGGAAGGCCG | GGGGCCTCGC | GCTCGGGCCC | 180     |
| CGGGCGGCGA  | CTGACAGCGG | CGGCGGCGGC                                  | GGCAGCGGCT | CCAAGGCGAG | CGTGGTCCCC | 240     |
| GCGTGCGCAC  | AAGCTCGCCG | CCGCGCAGGG                                  | ACCCACGGAC | ACCGGCGCCG | GGCGGACACA | 300     |
| CAGACGCGGA  | GATCGGGCTC | TACGCGCGCT                                  | ACTCAGCGCA | CGAGCTCCCC | ATCCCTGGGC | 360     |
| GGAGCGGGGC  | GCGGACTCGC | CGCTGCGCGC                                  | CCTCCCCGCG | GAGTCTGCC  | CGGGCAGACC | 420     |
| CGCAGCCCCG  | GGCCCCGCCG | CGAGGCCCT                                   | GGGTGAGCAG | CCTGTAGACA | CCTGGGGTTG | 480     |
| AGCAGTGGCG  | GCTGTGA    | ATG AGA GGC GGG CGG CAC TGG CCC GAG CCG CCT |            |            |            | 530     |
|   |            | Met Arg Gly Gly Arg His Trp Pro Glu Pro Pro |            |            |            |         |
|   |            | 1 5 10                                      |            |            |            |         |
| TGC AGG CTG AGA AGC GTC ATG GCC AGC ATC GCG CAG GTC TCC CTG GCT |            |   |            |            |            | 578     |
| Cys Arg Leu Arg Ser Val Met Ala Ser Ile Ala Gln Val Ser Leu Ala |            |   |            |            |            |         |
|   | 15         |   | 20         |            | 25         |         |
| GCT CTC CTC CTG CTG CCT ATG GCC ACC GCC ATG CAT TCC GAC TGC ATC |            |   |            |            |            | 626     |
| Ala Leu Leu Leu Leu Pro Met Ala Thr Ala Met His Ser Asp Cys Ile |            |   |            |            |            |         |
|   | 30         |   | 35 ▲       |            | 40         |         |
| TTC AAG AAG GAG CAA GCC ATG TGC CTG GAG AAG ATC CAG AGG GTG AAT |            |   |            |            |            | 674     |
| Phe Lys Lys Glu Gln Ala Met Cys Leu Glu Lys Ile Gln Arg Val Asn |            |   |            |            |            |         |
|   | 45         |   | 50         |            | 55         |         |
| GAC CTG ATG GGC TTG AAT GAC TCC TCC CCA GGG TGC CCT GGG ATG TGG |            |   |            |            |            | 722     |
| Asp Leu Met Gly Leu Asn Asp Ser Ser Pro Gly Cys Pro Gly Met Trp |            |   |            |            |            |         |
|   | 60         |   | 65         |            | 70         | 75      |
| GAC AAC ATC ACG TGT TGG AAG CCC GCC CAC GTG GGT GAG ATG GTC CTG |            |   |            |            |            | 770     |
| Asp Asn Ile Thr Cys Trp Lys Pro Ala His Val Gly Glu Met Val Leu |            |   |            |            |            |         |
|   |            | 80  |            |            | 85         | 90      |
| GTC AGT TGC CCT GAA CTC TTC CGA ATC TTC AAC CCA GAC CAA GTC TGG |            |   |            |            |            | 818     |
| Val Ser Cys Pro Glu Leu Phe Arg Ile Phe Asn Pro Asp Gln Val Trp |            |   |            |            |            |         |
|   |            | 95  |            |            | 100        | 105     |
| GAG ACG GAA ACC ATC GGA GAG TTC GGT TTT GCA GAC AGT AAA TCC TTG |            |   |            |            |            | 866     |
| Glu Thr Glu Thr Ile Gly Glu Phe Gly Phe Ala Asp Ser Lys Ser Leu |            |   |            |            |            |         |
|   | 110        |   |            |            | 115        | 120     |
| GAT CTC TCA GAC ATG AGG GTG GTG AGC CGG AAT TGC ACG GAG GAT GGA |            |   |            |            |            | 914     |
| Asp Leu Ser Asp Met Arg Val Val Ser Arg Asn Cys Thr Glu Asp Gly |            |   |            |            |            |         |
|   | 125        |   |            |            | 130        | 135     |
| TGG TCA GAG CCA TTC CCT CAT TAT TTC GAT GCC TGT GGG TTT GAG GAG |            |   |            |            |            | 962     |
| Trp Ser Glu Pro Phe Pro His Tyr Phe Asp Ala Cys Gly Phe Glu Glu |            |   |            |            |            |         |
|   | 140        |   |            |            | 145        | 150 155 |
| TAC GAA TCT GAG ACT GGG GAC CAG GAT TAC TAC TAC CTG TCA GTG AAG |            |   |            |            |            | 1010    |

FIG. 3A

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |      |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| Tyr | Glu | Ser | Glu | Thr | Gly | Asp | Gln | Asp | Tyr | Tyr | Tyr | Leu | Ser | Val | Lys |      |
|     |     |     |     | 160 |     |     |     |     | 165 |     |     |     |     | 170 |     |      |
| GCC | CTG | TAC | ACA | GTT | GGC | TAC | AGC | ACG | TCC | CTC | GTC | ACC | CTC | ACC | ACT | 1058 |
| Ala | Leu | Tyr | Thr | Val | Gly | Tyr | Ser | Thr | Ser | Leu | Val | Thr | Leu | Thr | Thr |      |
|     |     |     | 175 |     |     |     |     | 180 |     |     |     |     | 185 |     |     |      |
| GCC | ATG | GTC | ATC | CTG | TGT | CGT | TTC | CGG | AAG | CTG | CAC | TGC | ACC | CGC | AAC | 1106 |
| Ala | Met | Val | Ile | Leu | Cys | Arg | Phe | Arg | Lys | Leu | His | Cys | Thr | Arg | Asn |      |
|     |     | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     |     |     |      |
| TTC | ATC | CAC | ATG | AAC | CTC | TTC | GTG | TCG | TTT | ATG | CTG | AGG | GCC | ATC | TCC | 1154 |
| Phe | Ile | His | Met | Asn | Leu | Phe | Val | Ser | Phe | Met | Leu | Arg | Ala | Ile | Ser |      |
|     | 205 |     |     |     |     | 210 |     |     |     |     | 215 |     |     |     |     |      |
| GTC | TTC | ATC | AAA | GAC | TGG | ATC | CTC | TAT | GCT | GAG | CAG | GAC | AGC | AAT | CAC | 1202 |
| Val | Phe | Ile | Lys | Asp | Trp | Ile | Leu | Tyr | Ala | Glu | Gln | Asp | Ser | Asn | His |      |
|     | 220 |     |     |     | 225 |     |     |     |     | 230 |     |     |     |     | 235 |      |
| TGC | TTT | GTC | TCC | ACT | GTG | GAA | TGC | AAG | GCT | GTG | ATG | GTT | TTC | TTC | CAC | 1250 |
| Cys | Phe | Val | Ser | Thr | Val | Glu | Cys | Lys | Ala | Val | Met | Val | Phe | Phe | His |      |
|     |     |     |     | 240 |     |     |     |     | 245 |     |     |     |     | 250 |     |      |
| TAC | TGT | GTT | GTA | TCC | AAC | TAC | TTC | TGG | CTG | TTC | ATC | GAG | GGC | CTG | TAT | 1298 |
| Tyr | Cys | Val | Val | Ser | Asn | Tyr | Phe | Trp | Leu | Phe | Ile | Glu | Gly | Leu | Tyr |      |
|     |     |     | 255 |     |     |     |     | 260 |     |     |     |     | 265 |     |     |      |
| CTC | TTC | ACC | CTG | CTG | GTG | GAG | ACC | TTC | TTC | CCC | GAG | AGG | AGA | TAT | TTC | 1346 |
| Leu | Phe | Thr | Leu | Leu | Val | Glu | Thr | Phe | Phe | Pro | Glu | Arg | Arg | Tyr | Phe |      |
|     |     | 270 |     |     |     |     | 275 |     |     |     |     | 280 |     |     |     |      |
| TAC | TGG | TAC | ATC | ATC | ATT | GGC | TGG | GGG | ACA | CCA | ACT | GTG | TGT | GTG | TCT | 1394 |
| Tyr | Trp | Tyr | Ile | Ile | Ile | Gly | Trp | Gly | Thr | Pro | Thr | Val | Cys | Val | Ser |      |
|     | 285 |     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |     |      |
| GTG | TGG | GCT | ATG | CTG | AGG | CTC | TAC | TTC | GAT | GAC | ACA | GGC | TGC | TGG | GAT | 1442 |
| Val | Trp | Ala | Met | Leu | Arg | Leu | Tyr | Phe | Asp | Asp | Thr | Gly | Cys | Trp | Asp |      |
|     | 300 |     |     |     | 305 |     |     |     |     | 310 |     |     |     |     | 315 |      |
| ATG | AAT | GAC | AAC | ACG | GCT | CTG | TGG | TGG | GTG | ATC | AAA | GGC | CCT | GTA | GTT | 1490 |
| Met | Asn | Asp | Asn | Thr | Ala | Leu | Trp | Trp | Val | Ile | Lys | Gly | Pro | Val | Val |      |
|     |     |     |     | 320 |     |     |     |     | 325 |     |     |     |     | 330 |     |      |
| GGC | TCC | ATA | ATG | GTT | AAT | TTT | GTG | CTC | TTC | ATC | GGC | ATC | ATT | GTC | ATC | 1538 |
| Gly | Ser | Ile | Met | Val | Asn | Phe | Val | Leu | Phe | Ile | Gly | Ile | Ile | Val | Ile |      |
|     |     |     | 335 |     |     |     |     | 340 |     |     |     |     | 345 |     |     |      |
| CTT | GTG | CAG | AAA | CTT | CAG | TCT | CCA | GAC | ATG | GGA | GGC | AAC | GAG | TCC | AGC | 1586 |
| Leu | Val | Gln | Lys | Leu | Gln | Ser | Pro | Asp | Met | Gly | Gly | Asn | Glu | Ser | Ser |      |
|     |     | 350 |     |     |     |     | 355 |     |     |     |     | 360 |     |     |     |      |
| ATC | TAC | TTA | CGG | CTC | GCC | AGG | TCC | ACC | TTG | CTG | CTC | ATC | CCA | CTC | TTT | 1634 |
| Ile | Tyr | Leu | Arg | Leu | Ala | Arg | Ser | Thr | Leu | Leu | Leu | Ile | Pro | Leu | Phe |      |
|     | 365 |     |     |     |     | 370 |     |     |     |     | 375 |     |     |     |     |      |

FIG. 3B

|  |      |
|--|------|
| GGA ATC CAC TAC ACT GTC TTT GCT TTC TCC CCG GAG AAC GTC AGC AAG    | 1682 |
| Gly Ile His Tyr Thr Val Phe Ala Phe Ser Pro Glu Asn Val Ser Lys    |      |
| 380 385 390 395  |      |
| AGG GAG AGA CTG GTG TTT GAG CTG GGT CTG GGC TCC TTC CAG GGC TTT    | 1730 |
| Arg Glu Arg Leu Val Phe Glu Leu Gly Leu Gly Ser Phe Gln Gly Phe    |      |
| 400 405 410  |      |
| GTG GTG GCT GTT CTC TAT TGC TTT CTG AAT GGA GAG GTG CAG GCG GAG    | 1778 |
| Val Val Ala Val Leu Tyr Cys Phe Leu Asn Gly Glu Val Gln Ala Glu    |      |
| 415 420 425  |      |
| ATC AAG AGG AAG TGG CGG AGC TGG AAG GTG AAC CGC TAC TTC ACC ATG    | 1826 |
| Ile Lys Arg Lys Trp Arg Ser Trp Lys Val Asn Arg Tyr Phe Thr Met    |      |
| 430 435 440  |      |
| GAC TTC AAG CAC CGG CAC CCA TCC CTG GCC AGC AGC GGG GTG AAC GGG    | 1874 |
| Asp Phe Lys His Arg His Pro Ser Leu Ala Ser Ser Gly Val Asn Gly    |      |
| 445 450 455  |      |
| GGC ACC CAG CTC TCC ATC CTG AGC AAG AGC AGC TCC CAG ATC CGC ATG    | 1922 |
| Gly Thr Gln Leu Ser Ile Leu Ser Lys Ser Ser Ser Gln Ile Arg Met    |      |
| 460 465 470 475  |      |
| TCT GGG CTT CCG GCC GAC AAC CTG GCC ACC TGAGCCCACC CTGCCCCCTC CTCT | 1976 |
| Ser Gly Leu Pro Ala Asp Asn Leu Ala Thr                            |      |
| 480 485  |      |
| CCTCTGTACG CAGGCTGGGG CTGTGGTGGG GCGCCGGCCC ACGCATGTTG TGCCTCTTCT  | 2036 |
| CGCCTTCGGG CAGGCCCCGG GCTGGGCGCC TGGCCCCCGA GGTTGGAGAA GGATGCGGGA  | 2096 |
| CAGGCAGCTG TTTAGCCTTC CTGTTTTGGC GCTGGCCCAA CCACCGTGGG TCCCTGGGCC  | 2156 |
| TGCACCCAGA CATGTAATAC TCCTTAATTG GGAAGTCATC CATTCTTTCC CTTTCCCAAG  | 2216 |
| TCCTTGCTTA TTAAGAGGTT CAAGTCACCT ACCCAATTCA GAAGCTTAAG TAACCACTAA  | 2276 |
| CCACCGTGAC TGC GTGGGAG GCCTCCCATG GGCTGAGCTA CTGACTTGGC TTTGGGGGCC | 2336 |
| TTGGGCTGGG GCCCTCCTTA AAGCCCCCCC TGAAATTGTC GGACCTCAAA GTGTGACTCC  | 2396 |
| TTTGAGTCTA CTCGCCACCC CCGTGGCCCT TTGCAGCCCT GGTCCAGTCA CCGAGGTTAC  | 2456 |
| TGGAAGTCCA GCTTGGATGG CCAGACAGCT TTTTGGCACA GGCAGACCCA TGCTCACCCA  | 2516 |
| ACATTTTAGT GTCCAGGTGC CCAGGTGCCC AGGTGCCAG CTCCTGGGCA TCAGACAGTG   | 2576 |
| GGAAAGCTCC AGGGATCTAC CATTGAGAGA CTTGAGTTTG GATGTAGGGC TAAGGCCAGA  | 2636 |
| GAAAAGTTCT GGAGCTTTTC ATTTGGCCCA AGAAAAAACT GCCAAGATCC AGAAAAGTGG  | 2696 |
| ATCTGAGTGG AATTTAGATG CAAAGAGCTT GGAG                              | 2730 |

FIG. 3C

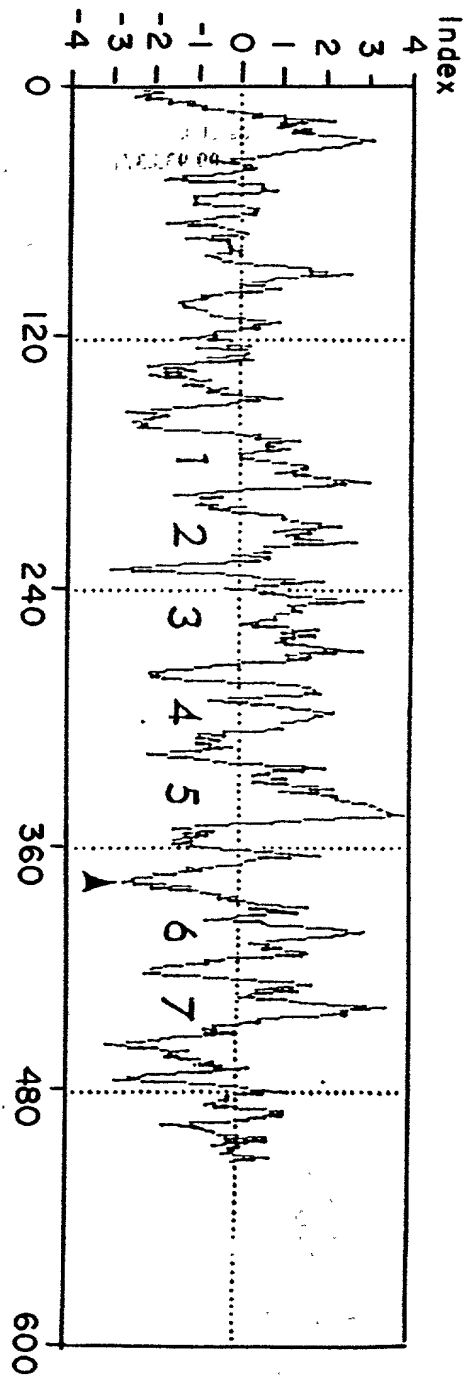


FIG. 5A

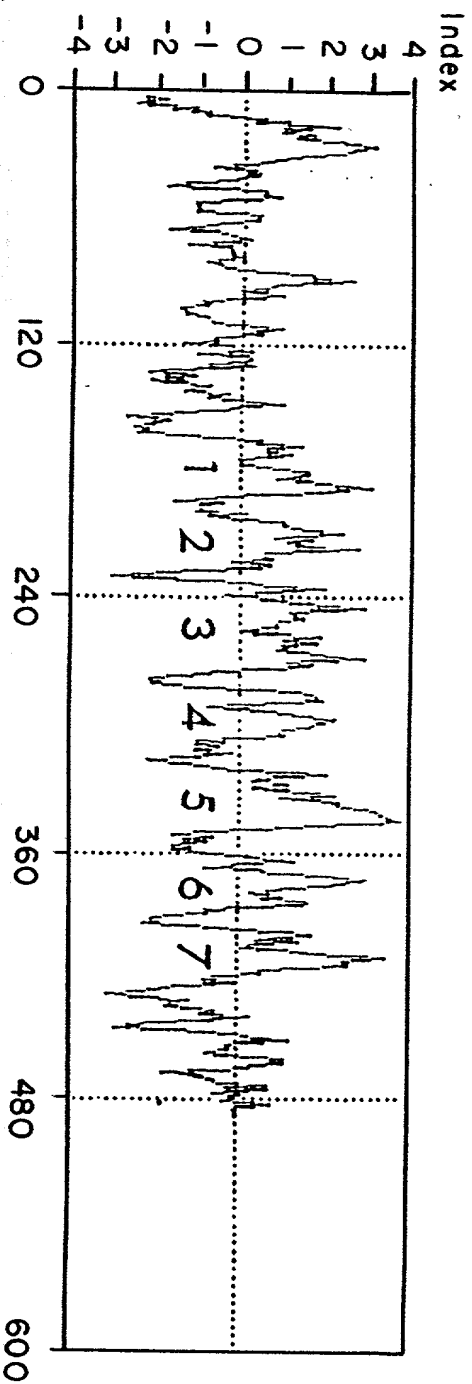


FIG. 5B



|   |     |
|---|-----|
| CGAGTGGACA GTGGCAGGCG GTGACTGAAT CTCCAAGTCT GGAAACAATA GCCAGAGATA | 60  |
| GTGGCTGGGA AGCACC ATG GCC AGA GTC CTG CAG CTC TCC CTG ACT GCT CTC | 112 |
| Met Ala Arg Val Leu Gln Leu Ser Leu Thr Ala Leu                   |     |
| 1 5 10  |     |
| CTG CTG CCT GTG GCT ATT GCT ATG CAC TCT GAC TGC ATC TTC AAG AAG   | 160 |
| Leu Leu Pro Val Ala Ile Ala Met His Ser Asp Cys Ile Phe Lys Lys   |     |
| 15 20 25  |     |
| GAG CAA GCC ATG TGC CTG GAG AGG ATC CAG AGG GCC AAC GAC CTG ATG   | 208 |
| Glu Gln Ala Met Cys Leu Glu Arg Ile Gln Arg Ala Asn Asp Leu Met   |     |
| 30 35 40  |     |
| GGA CTA AAC GAG TCT TCC CCA GGT TGC CCT GGC ATG TGG GAC AAT ATC   | 256 |
| Gly Leu Asn Glu Ser Ser Pro Gly Cys Pro Gly Met Trp Asp Asn Ile   |     |
| 45 50 55 60   |     |
| ACA TGT TGG AAG CCA GCT CAA GTA GGT GAG ATG GTC CTT GTA AGC TGC   | 304 |
| Thr Cys Trp Lys Pro Ala Gln Val Gly Glu Met Val Leu Val Ser Cys   |     |
| 65 70 75  |     |
| CCT GAG GTC TTC CGG ATC TTC AAC CCG GAC CAA GTC TGG ATG ACA GAA   | 352 |
| Pro Glu Val Phe Arg Ile Phe Asn Pro Asp Gln Val Trp Met Thr Glu   |     |
| 80 85 90  |     |
| ACC ATA GGA GAT TCT GGT TTT GCC GAT AGT AAT TCC TTG GAG ATC ACA   | 400 |
| Thr Ile Gly Asp Ser Gly Phe Ala Asp Ser Asn Ser Leu Glu Ile Thr   |     |
| 95 100 105  |     |
| GAC ATG GGG GTC GTG GGC CGG AAC TGC ACA GAG GAC GGC TGG TCG GAG   | 448 |
| Asp Met Gly Val Val Gly Arg Asn Cys Thr Glu Asp Gly Trp Ser Glu   |     |
| 110 115 120   |     |
| CCC TTC CCC CAC TAC TTC GAT GCT TGT GGG TTT GAT GAT TAT GAG CCT   | 496 |
| Pro Phe Pro His Tyr Phe Asp Ala Cys Gly Phe Asp Asp Tyr Glu Pro   |     |
| 125 130 135 140   |     |
| GAG TCT GGA GAT CAG GAT TAT TAC TAC CTG TCG GTG AAG GCT CTC TAC   | 544 |
| Glu Ser Gly Asp Gln Asp Tyr Tyr Tyr Leu Ser Val Lys Ala Leu Tyr   |     |
| 145 150 155   |     |
| ACA GTC GGC TAC AGC ACT TCC CTC GCC ACC CTC ACT ACT GCC ATG GTC   | 592 |
| Thr Val Gly Tyr Ser Thr Ser Leu Ala Thr Leu Thr Thr Ala Met Val   |     |
| 160 165 170   |     |
| ATC TTG TGC CGC TTC CGG AAG CTG CAT TGC ACT CGC AAC TTC ATC CAC   | 640 |
| Ile Leu Cys Arg Phe Arg Lys Leu His Cys Thr Arg Asn Phe Ile His   |     |
| 175 180 185   |     |
| ATG AAC CTG TTT GTA TCC TTC ATG CTG AGG GCT ATC TCC GTC TTC ATC   | 688 |
| Met Asn Leu Phe Val Ser Phe Met Leu Arg Ala Ile Ser Val Phe Ile   |     |

FIG. 7A

| 190               | 195               | 200               |      |
|-------------------|-------------------|-------------------|------|
| AAG<br>Lys<br>205 | GAC<br>Asp<br>210 | TGG<br>Trp<br>215 | 736  |
| ATC<br>Ile        | TTG<br>Leu        | TAC<br>Tyr        |      |
| GCC<br>Ala        | GAG<br>Glu        | CAG<br>Gln        |      |
| GAC<br>Asp        | AGC<br>Ser        | AGT<br>Ser        |      |
| CAC<br>His        | TGC<br>Cys        | TTC<br>Phe        |      |
| GTT<br>Val        |                   |                   |      |
| TCC<br>Ser        | ACC<br>Thr        | GTG<br>Val        | 784  |
| GAG<br>Glu        | TGC<br>Cys        | AAA<br>Lys        |      |
| GCT<br>Ala        | GTC<br>Val        | ATG<br>Met        |      |
| GTT<br>Val        | TTC<br>Phe        | TTC<br>Phe        |      |
| CAC<br>His        | TAC<br>Tyr        | TGC<br>Cys        |      |
| GTG<br>Val        |                   |                   |      |
| TCC<br>Ser        | AAC<br>Asn        | TAC<br>Tyr        | 832  |
| TTC<br>Phe        | TGG<br>Trp        | CTG<br>Leu        |      |
| CTG<br>Leu        | TTC<br>Phe        | ATT<br>Ile        |      |
| GAA<br>Glu        | GGC<br>Gly        | CTG<br>Leu        |      |
| TAC<br>Tyr        | CTC<br>Leu        | TTT<br>Phe        |      |
| ACA<br>Thr        |                   |                   |      |
| CTG<br>Leu        | CTG<br>Leu        | GAG<br>Glu        | 880  |
| ACC<br>Thr        | TTC<br>Phe        | TTC<br>Phe        |      |
| CCT<br>Pro        | GAG<br>Glu        | AGG<br>Arg        |      |
| AGA<br>Arg        | TAT<br>Tyr        | TTC<br>Phe        |      |
| TAC<br>Tyr        | TGG<br>Trp        | TAC<br>Tyr        |      |
| GTT<br>Val        |                   |                   |      |
| ACC<br>Thr        | ATC<br>Ile        | ATC<br>Ile        | 928  |
| ATC<br>Ile        | GAG<br>Glu        | TGG<br>Trp        |      |
| GGC<br>Gly        | TGG<br>Trp        | GGG<br>Gly        |      |
| ACA<br>Thr        | CCT<br>Pro        | ACT<br>Thr        |      |
| GTT<br>Val        | GTA<br>Val        | ACA<br>Thr        |      |
| GTG<br>Val        | TGG<br>Trp        | GCT<br>Ala        |      |
| GAT<br>Asp        | GAT<br>Asp        | GCA<br>Ala        | 976  |
| GGA<br>Gly        | TGC<br>Cys        | TGG<br>Trp        |      |
| GAT<br>Asp        | ATG<br>Met        | AAT<br>Asn        |      |
| GAC<br>Asp        |                   |                   |      |
| AGC<br>Ser        | ACA<br>Thr        | GCT<br>Ala        | 1024 |
| CTG<br>Leu        | TGG<br>Trp        | TGG<br>Trp        |      |
| GTG<br>Val        | ATC<br>Ile        | AAA<br>Lys        |      |
| GGC<br>Gly        | CCC<br>Pro        | GTG<br>Val        |      |
| GTT<br>Val        | GGC<br>Gly        | TCT<br>Ser        |      |
| ATA<br>Ile        |                   |                   |      |
| ATG<br>Met        | GTT<br>Val        | AAC<br>Asn        | 1072 |
| TTT<br>Phe        | GTG<br>Val        | CTT<br>Leu        |      |
| TTC<br>Phe        | ATC<br>Ile        | GGC<br>Gly        |      |
| ATC<br>Ile        | ATC<br>Ile        | ATC<br>Ile        |      |
| ATC<br>Ile        | CTT<br>Leu        | GTA<br>Val        |      |
| CAG<br>Gln        |                   |                   |      |
| AAG<br>Lys        | CTG<br>Leu        | CAG<br>Gln        | 1120 |
| TCC<br>Ser        | CCA<br>Pro        | GAC<br>Asp        |      |
| ATG<br>Met        | GGA<br>Gly        | GGC<br>Gly        |      |
| AAC<br>Asn        | GAG<br>Glu        | TCC<br>Ser        |      |
| AGC<br>Ser        | ATC<br>Ile        | TAC<br>Tyr        |      |
| TTA<br>Leu        |                   |                   |      |
| CGG<br>Arg        | CTG<br>Leu        | CTC<br>Leu        | 1168 |
| GCC<br>Ala        | CGC<br>Arg        | TCC<br>Ser        |      |
| ACC<br>Thr        | CTA<br>Leu        | CTG<br>Leu        |      |
| CTC<br>Leu        | ATC<br>Ile        | CCA<br>Pro        |      |
| CTC<br>Leu        | TTC<br>Phe        | GGA<br>Gly        |      |
| ATC<br>Ile        | CAC<br>His        |                   |      |
| TAC<br>Tyr        | ACA<br>Thr        | GTA<br>Val        | 1216 |
| TTC<br>Phe        | GCC<br>Ala        | TTC<br>Phe        |      |
| TCT<br>Ser        | CCA<br>Pro        | GAG<br>Glu        |      |
| AAC<br>Asn        | GTC<br>Val        | AGC<br>Ser        |      |
| AGC<br>Ser        | AAG<br>Lys        | AGG<br>Arg        |      |
| GAA<br>Glu        | AGA<br>Arg        |                   |      |
| GCT<br>Ala        |                   |                   |      |
| CTT<br>Leu        | GTG<br>Val        | TTT<br>Phe        | 1264 |
| GAG<br>Glu        | CTT<br>Leu        | GGG<br>Gly        |      |
| CTG<br>Leu        | GGC<br>Gly        | TCC<br>Ser        |      |
| TTC<br>Phe        | CAG<br>Gln        | GGC<br>Gly        |      |
| TTT<br>Phe        | GTG<br>Val        | GTG<br>Val        |      |
| GCT<br>Ala        |                   |                   |      |
| GTA<br>Val        | CTC<br>Leu        | TAC<br>Tyr        | 1312 |
| TGC<br>Cys        | TTC<br>Phe        | CTG<br>Leu        |      |
| AAT<br>Asn        | GGG<br>Gly        | GAG<br>Glu        |      |
| GTA<br>Val        | CAG<br>Gln        | GCA<br>Ala        |      |
| GAG<br>Glu        | ATT<br>Ile        | AAG<br>Lys        |      |
| AGG<br>Arg        |                   |                   |      |

FIG. 7B

|   |      |
|---|------|
| AAA TGG AGG AGC TGG AAG GTG AAC CGT TAC TTC ACT ATG GAC TTC AAG   | 1360 |
| Lys Trp Arg Ser Trp Lys Val Asn Arg Tyr Phe Thr Met Asp Phe Lys   |      |
| 415 420 425   |      |
| CAC CGG CAC CCG TCC CTG GCC AGC AGT GGA GTA AAT GGG GGA ACC CAG   | 1408 |
| His Arg His Pro Ser Leu Ala Ser Ser Gly Val Asn Gly Gly Thr Gln   |      |
| 430 435 440   |      |
| CTG TCC ATC CTG AGC AAG AGC AGC TCC CAG CTC CGC ATG TCC AGC CTC   | 1456 |
| Leu Ser Ile Leu Ser Lys Ser Ser Ser Gln Leu Arg Met Ser Ser Leu   |      |
| 445 450 455 460   |      |
| CCG GCC GAC AAC TTG GCC ACC TGAGGCCTGT CTCCTCCTC CTTCTGCACA GGCTG | 1512 |
| Pro Ala Asp Asn Leu Ala Thr ***                                   |      |
| 465   |      |
| GGGCTGCGGG CCAGTGCCTG AGCATGTTTG TGCCTCTCCC CTCTCCTTGG GCAGGCCCTG | 1572 |
| GGTAGGAAGC TGGGCTCCTC CCCAAAGGGG AAGAGAGAGA TAGGGTATAG GCTGATATTG | 1632 |
| CTCCTCCTGT TTGGGTCCCA CCTACTGTGA TTCATTGAGC CTGATTTGAC ATGTAAATAC | 1692 |
| ACCTCAAATT TGGAAAGTTG CCCCATCTCT GCCCCCAACC CATGCCCTG CTCACCTCTG  | 1752 |
| CCAGGCCCCA GCTCAACCTA CTGTGTCAAG GCCAGCCTCA GTGATAGTCT GATCCCAGGT | 1812 |
| ACAAGGCCTT GTGAGCTGAG GCTGAAAGGC CTGTTTTGGA GAGGCTGGGG TAGTGCC    | 1869 |

FIG. 8

|   |     |
|---|-----|
| CGAGTGGACA GTGGCAGGCG GTGACTGAAT CTCCAAGTCT GGAAACAATA GCCAGAGATA | 60  |
| GTGGCTGGGA AGCACC ATG GCC AGA GTC CTG CAG CTC TCC CTG ACT GCT CTC | 112 |
| Met Ala Arg Val Leu Gln Leu Ser Leu Thr Ala Leu                   |     |
| 1 5 10  |     |
| CTG CTG CCT GTG GCT ATT GCT ATG CAC TCT GAC TGC ATC TTC AAG AAG   | 160 |
| Leu Leu Pro Val Ala Ile Ala Met His Ser Asp Cys Ile Phe Lys Lys   |     |
| 15 20 25  |     |
| GAG CAA GCC ATG TGC CTG GAG AGG ATC CAG AGG GCC AAC GAC CTG ATG   | 208 |
| Glu Gln Ala Met Cys Leu Glu Arg Ile Gln Arg Ala Asn Asp Leu Met   |     |
| 30 35 40  |     |
| GGA CTA AAC GAG TCT TCC CCA GGT TGC CCT GGC ATG TGG GAC AAT ATC   | 256 |
| Gly Leu Asn Glu Ser Ser Pro Gly Cys Pro Gly Met Trp Asp Asn Ile   |     |
| 45 50 55 60   |     |
| ACA TGT TGG AAG CCA GCT CAA GTA GGT GAG ATG GTC CTT GTA AGC TGC   | 304 |
| Thr Cys Trp Lys Pro Ala Gln Val Gly Glu Met Val Leu Val Ser Cys   |     |
| 65 70 75  |     |
| CCT GAG GTC TTC CGG ATC TTC AAC CCG GAC CAA GTC TGG ATG ACA GAA   | 352 |
| Pro Glu Val Phe Arg Ile Phe Asn Pro Asp Gln Val Trp Met Thr Glu   |     |
| 80 85 90  |     |
| ACC ATA GGA GAT TCT GGT TTT GCC GAT AGT AAT TCC TTG GAG ATC ACA   | 400 |
| Thr Ile Gly Asp Ser Gly Phe Ala Asp Ser Asn Ser Leu Glu Ile Thr   |     |
| 95 100 105  |     |
| GAC ATG GGG GTC GTG GGC CGG AAC TGC ACA GAG GAC GGC TGG TCG GAG   | 448 |
| Asp Met Gly Val Val Gly Arg Asn Cys Thr Glu Asp Gly Trp Ser Glu   |     |
| 110 115 120   |     |
| CCC TTC CCC CAC TAC TTC GAT GCT TGT GGG TTT GAT GAT TAT GAG CCT   | 496 |
| Pro Phe Pro His Tyr Phe Asp Ala Cys Gly Phe Asp Asp Tyr Glu Pro   |     |
| 125 130 135 140   |     |
| GAG TCT GGA GAT CAG GAT TAT TAC TAC CTG TCG GTG AAG GCT CTC TAC   | 544 |
| Glu Ser Gly Asp Gln Asp Tyr Tyr Tyr Leu Ser Val Lys Ala Leu Tyr   |     |
| 145 150 155   |     |
| ACA GTC GGC TAC AGC ACT TCC CTC GCC ACC CTC ACT ACT GCC ATG GTC   | 592 |
| Thr Val Gly Tyr Ser Thr Ser Leu Ala Thr Leu Thr Thr Ala Met Val   |     |
| 160 165 170   |     |
| ATC TTG TGC CGC TTC CGG AAG CTG CAT TGC ACT CGC AAC TTC ATC CAC   | 640 |
| Ile Leu Cys Arg Phe Arg Lys Leu His Cys Thr Arg Asn Phe Ile His   |     |
| 175 180 185   |     |
| ATG AAC CTG TTT GTA TCC TTC ATG CTG AGG GCT ATC TCC GTC TTC ATC   | 688 |
| Met Asn Leu Phe Val Ser Phe Met Leu Arg Ala Ile Ser Val Phe Ile   |     |
| 190 195 200   |     |

FIG. 9A

|                   |            |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |      |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| AAG<br>Lys<br>205 | GAC<br>Asp | TGG<br>Trp        | ATC<br>Ile        | TTG<br>Leu        | TAC<br>Tyr<br>210 | GCC<br>Ala        | GAG<br>Glu        | CAG<br>Gln        | GAC<br>Asp<br>215 | AGC<br>Ser        | AGT<br>Ser        | CAC<br>His        | TGC<br>Cys        | TTC<br>Phe        | GTT<br>Val<br>220 | 736  |
| TCC<br>Ser        | ACC<br>Thr | GTG<br>Val        | GAG<br>Glu        | TGC<br>Cys<br>225 | AAA<br>Lys        | GCT<br>Ala        | GTC<br>Val        | ATG<br>Met        | GTT<br>Val<br>230 | TTC<br>Phe        | TTC<br>Phe        | CAC<br>His        | TAC<br>Tyr        | TGC<br>Cys<br>235 | GTG<br>Val        | 784  |
| GTG<br>Val        | TCC<br>Ser | AAC<br>Asn        | TAC<br>Tyr<br>240 | TTT<br>Phe        | TGG<br>Trp        | CTG<br>Leu        | TTC<br>Phe        | ATT<br>Ile<br>245 | GAA<br>Glu        | GGC<br>Gly        | CTG<br>Leu        | TAC<br>Tyr        | CTC<br>Leu<br>250 | TTT<br>Phe        | ACA<br>Thr        | 832  |
| CTG<br>Leu        | CTG<br>Leu | GTG<br>Val<br>255 | GAG<br>Glu        | ACC<br>Thr        | TTC<br>Phe        | TTC<br>Phe        | CCT<br>Pro<br>260 | GAG<br>Glu        | AGG<br>Arg        | AGA<br>Arg        | TAT<br>Tyr        | TTC<br>Phe<br>265 | TAC<br>Tyr        | TGG<br>Trp        | TAC<br>Tyr        | 880  |
| ACC<br>Thr<br>270 | ATC<br>Ile | ATC<br>Ile        | GGC<br>Gly        | TGG<br>Trp        | GGG<br>Gly        | ACA<br>Thr<br>275 | CCT<br>Pro        | ACT<br>Thr        | GTG<br>Val        | TGT<br>Cys        | GTA<br>Val<br>280 | ACA<br>Thr        | GTG<br>Val        | TGG<br>Trp        | GCT<br>Ala        | 928  |
| GTG<br>Val<br>285 | CTG<br>Leu | AGG<br>Arg        | CTC<br>Leu        | TAT<br>Tyr        | TTT<br>Phe<br>290 | GAT<br>Asp        | GAT<br>Asp        | GCA<br>Ala        | GGA<br>Gly        | TGC<br>Cys<br>295 | TGG<br>Trp        | GAT<br>Asp        | ATG<br>Met        | AAT<br>Asn        | GAC<br>Asp<br>300 | 976  |
| AGC<br>Ser        | ACA<br>Thr | GCT<br>Ala        | CTG<br>Leu        | TGG<br>Trp<br>305 | TGG<br>Trp        | GTG<br>Val        | ATC<br>Ile        | AAA<br>Lys        | GGC<br>Gly<br>310 | CCC<br>Pro        | GTG<br>Val        | GTT<br>Val        | GGC<br>Gly        | TCT<br>Ser<br>315 | ATA<br>Ile        | 1024 |
| ATG<br>Met        | GTT<br>Val | AAC<br>Asn        | TTT<br>Phe<br>320 | GTG<br>Val        | CTT<br>Leu        | TTC<br>Phe        | ATC<br>Ile        | GGC<br>Gly<br>325 | ATC<br>Ile        | ATC<br>Ile        | ATC<br>Ile        | ATC<br>Ile        | CTT<br>Leu<br>330 | GTA<br>Val        | CAG<br>Gln        | 1072 |
| AAG<br>Lys        | CTG<br>Leu | CAG<br>Gln<br>335 | TCC<br>Ser        | CCA<br>Pro        | GAC<br>Asp        | ATG<br>Met        | GGA<br>Gly<br>340 | GGC<br>Gly        | AAC<br>Asn        | GAG<br>Glu        | TCC<br>Ser        | AGC<br>Ser<br>345 | ATC<br>Ile        | TAC<br>Tyr        | TTT<br>Phe<br>△   | 1120 |
| AGC<br>Ser<br>350 | TGC<br>Cys | GTG<br>Val        | CAG<br>Gln        | AAA<br>Lys        | TGC<br>Cys        | TAC<br>Tyr<br>355 | TGC<br>Cys        | AAG<br>Lys        | CCA<br>Pro        | CAG<br>Gln        | CGG<br>Arg<br>360 | GCT<br>Ala        | CAG<br>Gln        | CAG<br>Gln        | CAC<br>His        | 1168 |
| TCT<br>Ser<br>365 | TGC<br>Cys | AAG<br>Lys        | ATG<br>Met        | TCA<br>Ser        | GAA<br>Glu        | CTA<br>Leu<br>370 | TCC<br>Ser        | ACC<br>Thr        | ATT<br>Ile        | ACT<br>Thr<br>375 | CTA<br>Leu<br>△   | CGG<br>Arg        | CTG<br>Leu        | GCC<br>Ala        | CGC<br>Arg<br>380 | 1216 |
| TCC<br>Ser        | ACC<br>Thr | CTA<br>Leu        | CTG<br>Leu        | CTC<br>Leu        | ATC<br>Ile        | CCA<br>Pro        | CTC<br>Leu        | TTC<br>Phe        | GGA<br>Gly<br>390 | ATC<br>Ile        | CAC<br>His        | TAC<br>Tyr        | ACA<br>Thr        | GTA<br>Val<br>395 | TTT<br>Phe        | 1264 |
| GCC<br>Ala        | TTC<br>Phe | TCT<br>Ser        | CCA<br>Pro<br>400 | GAG<br>Glu        | AAC<br>Asn        | GTC<br>Val        | AGC<br>Ser        | AAG<br>Lys<br>405 | AGG<br>Arg        | GAA<br>Glu        | AGA<br>Arg        | CTT<br>Leu        | GTG<br>Val<br>410 | TTT<br>Phe        | GAG<br>Glu        | 1312 |
| CTT<br>Leu        | GGG<br>Gly | CTG<br>Leu        | GGC<br>Gly        | TCC<br>Ser        | TTC<br>Phe        | CAG<br>Gln        | GGC<br>Gly        | TTT<br>Phe        | GTG<br>Val        | GTG<br>Val        | GCT<br>Ala        | GTA<br>Val        | CTC<br>Leu        | TAC<br>Tyr        | TGC<br>Cys        | 1360 |

FIG. 9B

| 415  | 420 | 425 |      |
|--|-----|-----|------|
| TTC CTG AAT GGG GAG GTA CAG GCA GAG ATT AAG AGG AAA TGG AGG AGC    |     |     | 1408 |
| Phe Leu Asn Gly Glu Val Gln Ala Glu Ile Lys Arg Lys Trp Arg Ser    |     |     |      |
| 430  | 435 | 440 |      |
| TGG AAG GTG AAC CGT TAC TTC ACT ATG GAC TTC AAG CAC CGG CAC CCG    |     |     | 1456 |
| Trp Lys Val Asn Arg Tyr Phe Thr Met Asp Phe Lys His Arg His Pro    |     |     |      |
| 445  | 450 | 455 | 460  |
| TCC CTG GCC AGC AGT GGA GTA AAT GGG GGA ACC CAG CTG TCC ATC CTG    |     |     | 1504 |
| Ser Leu Ala Ser Ser Gly Val Asn Gly Gly Thr Gln Leu Ser Ile Leu    |     |     |      |
|  | 465 | 470 | 475  |
| AGC AAG AGC AGC TCC CAG CTC CGC ATG TCC AGC CTC CCG GCC GAC AAC    |     |     | 1552 |
| Ser Lys Ser Ser Ser Gln Leu Arg Met Ser Ser Leu Pro Ala Asp Asn    |     |     |      |
|  | 480 | 485 | 490  |
| TTG GCC ACC TGAGGCCTGT CTCCCTCCTC CTTCTGCACA GGCTGGGGCT GCGGGCCAGT |     |     | 1611 |
| Leu Ala Thr ***  |     |     |      |
| 495  |     |     |      |
| GCCTGAGCAT GTTTGTGCCT CTCCCCTCTC CTTGGGCAGG CCCTGGGTAG GAAGCTGGGC  |     |     | 1671 |
| TCCTCCCCAA AGGGGAAGAG AGAGATAGGG TATAGGCTGA TATTGCTCCT CCTGTTTGGG  |     |     | 1731 |
| TCCCACCTAC TGTGATTCAT TGAGCCTGAT TTGACATGTA AATACACCTC AAATTTGGAA  |     |     | 1791 |
| AGTTGCCCCA TCTCTGCCCC CAACCCATGC CCCTGCTCAC CTCTGCCAGG CCCCAGCTCA  |     |     | 1851 |
| ACCTACTGTG TCAAGGCCAG CCTCAGTGAT AGTCTGATCC CAGGTACAAG GCCTTGTGAG  |     |     | 1911 |
| CTGAGGCTGA AAGGCCTGTT TTGGAGAGGC TGGGGTAGTG CCCACCCAG CAGCCTTTCA   |     |     | 1971 |
| GCAAATTGAC TTTGGATGTG GACCCCTTCTC AGCCTGTACC AAGTACTGCA GTTGGCTAGG |     |     | 2031 |
| GATGCAGCTC AGTTTCCTGA GCATCCTTTG GAGCAGGTCA ACCTGAGGCT CCTTTTGCTT  |     |     | 2091 |
| ACCCGACATC TAAGTTGTCC AGGTGCTCGG CTCCTGTGTG CCTGGATGAC GGGAGGGCTC  |     |     | 2151 |
| CGGGGTCTTT CAGTCAAAGA CTTACATTGA GGTGGGGTGA GAGTCAGAGA AAAGTTCTGG  |     |     | 2211 |
| TGCTTTTCAT TTGTTCTAAG AGCTGAGAGC CAGGAATGCA GAGTCAATTG GGAAGGAGAT  |     |     | 2271 |
| GGGATAGCTG ATGATCTTAC CATGTCCATG ACTGTGCCCC TGATTCAAGA CCGGATCATG  |     |     | 2331 |
| TGGTGGCTTT ATTTCTACAC TTCTTGTTCCA CAATGGACAG TCTGAGGAAG CTCTTCTTTC |     |     | 2391 |
| AGCCACAACA ACCACAGAAA GCCCTTTCTT CTCCCCTCTT GTTCTCCAT AAGTCAAAGC   |     |     | 2451 |
| CATGTTTAGA ACGGACCAGC CACCTTGCGA TGAATCACT GAGTTCTGAA GCAACTTTCA   |     |     | 2511 |
| ATTTCCACGA GCCAAGTCCT GGGTCCAGGG ACGCCCC                           |     |     | 2548 |

FIG. 10

|        |   |
|--------|---|
| Rat    | Met His Ser Asp Cys Ile Phe Lys Lys Glu Gln Ala Met Cys Leu Glu |
|        | * * * * *   |
| Bovine | Met His Ser Asp Cys Ile Phe Lys Lys Glu Gln Ala Met Cys Leu Glu |
|        | 1 5 10 15   |
| Rat    | Arg Ile Gln Arg Ala Asn Asp Leu Met Gly Leu Asn Glu             |
|        | * * * * *   |
| Bovine | Lys Ile Gln Arg Val Asn Asp Leu Met Gly Leu Asn Asp             |
|        | 20 25   |

FIG. 11

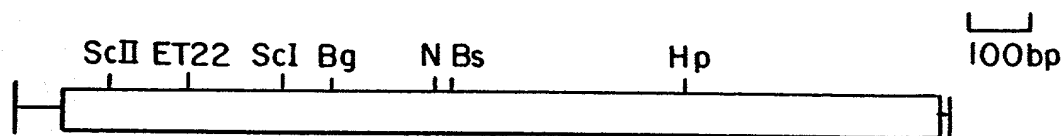


FIG. 12

|        |   |
|--------|---|
| Human  | Met His Ser Asp Cys Ile Phe Lys Lys Glu Gln Ala Met Cys Leu |
|        | * * * * *   |
| Bovine | Met His Ser Asp Cys Ile Phe Lys Lys Glu Gln Ala Met Cys Leu |
| Human  | Gly Lys Ile Gln Arg Ala Asn Glu Leu Met Gly Phe Asn Asp     |
|        | * * * * *   |
| Bovine | Glu Lys Ile Gln Arg Val Asn Asp Leu Met Gly Leu Asn Asp     |

FIG. 14

|   |     |
|---|-----|
| AGCCCAGAGA CACATTGGGG CTGACCTGCC GCTGCTGTCA GTGGGAGGCC AGTGGTGCTG | 60  |
| GCCAAGAAGT GTC ATG GCT GGT GTC GTG CAC GTT TCC CTG GCT GCT CAC    | 109 |
| Met Ala Gly Val Val His Val Ser Leu Ala Ala His                   |     |
| 1 5 10  |     |
| TGC GGG GCC TGT CCG TGG GGC CGG GGC AGA CTC CGC AAA GGA CGC GCA   | 157 |
| Cys Gly Ala Cys Pro Trp Gly Arg Gly Arg Leu Arg Lys Gly Arg Ala   |     |
| 15 20 25  |     |
| GCC TGC AAG TCC GCG GCC CAG AGA CAC ATT GGG GCT GAC CTG CCG CTG   | 205 |
| Ala Cys Lys Ser Ala Ala Gln Arg His Ile Gly Ala Asp Leu Pro Leu   |     |
| 30 35 40  |     |
| CTG TCA GTG GGA GGC CAG TGG TGC TGG CCA AGA AGT GTC ATG GCT GGT   | 253 |
| Leu Ser Val Gly Gly Gln Trp Cys Trp Pro Arg Ser Val Met Ala Gly   |     |
| 45 50 55 60   |     |
| GTC GTG CAC GTT TCC CTG GCT GCT CTC CTC CTG CTG CCT ATG GCC CCT   | 301 |
| Val Val His Val Ser Leu Ala Ala Leu Leu Leu Leu Pro Met Ala Pro   |     |
| 65 70 75  |     |
| GCC ATG CAT TCT GAC TGC ATC TTC AAG AAG GAG CAA GCC ATG TGC CTG   | 349 |
| Ala Met His Ser Asp Cys Ile Phe Lys Lys Glu Gln Ala Met Cys Leu   |     |
| 80 85 90  |     |
| GAG AAG ATC CAG AGG GCC AAT GAG CTG ATG GGC TTC AAT GAT TCC TCT   | 397 |
| Glu Lys Ile Gln Arg Ala Asn Glu Leu Met Gly Phe Asn Asp Ser Ser   |     |
| 95 100 105  |     |
| CCA GGC TGT CCT GGG ATG TGG GAC AAC ATC ACG TGT TGG AAG CCC GCC   | 445 |
| Pro Gly Cys Pro Gly Met Trp Asp Asn Ile Thr Cys Trp Lys Pro Ala   |     |
| 110 115 120   |     |
| CAT GTG GGT GAG ATG GTC CTG GTC AGC TGC CCT GAG CTC TTC CGA ATC   | 493 |
| His Val Gly Glu Met Val Leu Val Ser Cys Pro Glu Leu Phe Arg Ile   |     |
| 125 130 135 140   |     |
| TTC AAC CCA GAC CAA GTC TGG GAG ACC GAA ACC ATT GGA GAG TCT GAT   | 541 |
| Phe Asn Pro Asp Gln Val Trp Glu Thr Glu Thr Ile Gly Glu Ser Asp   |     |
| 145 150 155   |     |
| TTT GGT GAC AGT AAC TCC TTA GAT CTC TCA GAC ATG GGA GTG GTG AGC   | 589 |
| Phe Gly Asp Ser Asn Ser Leu Asp Leu Ser Asp Met Gly Val Val Ser   |     |
| 160 165 170   |     |
| CGG AAC TGC ACG GAG GAT GGC TGG TCG GAA CCC TTC CCT CAT TAC TTT   | 637 |
| Arg Asn Cys Thr Glu Asp Gly Trp Ser Glu Pro Phe Pro His Tyr Phe   |     |
| 175 180 185   |     |
| GAT GCC TGT GGG TTT GAT GAA TAT GAA TCT GAG ACT GGG GAC CAG GAT   | 685 |
| Asp Ala Cys Gly Phe Asp Glu Tyr Glu Ser Glu Thr Gly Asp Gln Asp   |     |

FIG. 13A



| 190   | 195  | 200 |  |
|---|------|-----|--|
| TAT TAC TAC CTG TCA GTG AAG GCC CTC TAC ACG GTT GGC TAC AGC ACA<br>Tyr Tyr Tyr Leu Ser Val Lys Ala Leu Tyr Thr Val Gly Tyr Ser Thr<br>205 210 215 220 | 733  |     |  |
| TCC CTC GTC ACC CTC ACC ACT GCC ATG GTC ATC CTT TGT CGC TTC CGG<br>Ser Leu Val Thr Leu Thr Thr Ala Met Val Ile Leu Cys Arg Phe Arg<br>225 230 235     | 781  |     |  |
| AAG CTG CAC TGC ACA CGC AAC TTC ATC CAC ATG AAC CTG TTT GTG TCG<br>Lys Leu His Cys Thr Arg Asn Phe Ile His Met Asn Leu Phe Val Ser<br>240 245 250     | 829  |     |  |
| TTC ATG CTG AGG GCG ATC TCC GTC TTC ATC AAA GAC TGG ATT CTG TAT<br>Phe Met Leu Arg Ala Ile Ser Val Phe Ile Lys Asp Trp Ile Leu Tyr<br>255 260 265     | 877  |     |  |
| GCG GAG CAG GAC AGC AAC CAC TGC TTC ATC TCC ACT GTG GAA TGT AAG<br>Ala Glu Gln Asp Ser Asn His Cys Phe Ile Ser Thr Val Glu Cys Lys<br>270 275 280     | 925  |     |  |
| GCC GTC ATG GTT TTC TTC CAC TAC TGT GTT GTG TCC AAC TAC TTC TGG<br>Ala Val Met Val Phe Phe His Tyr Cys Val Val Ser Asn Tyr Phe Trp<br>285 290 295 300 | 973  |     |  |
| CTG TTC ATC GAG GGC CTG TAC CTC TTC ACT CTG CTG GTG GAG ACC TTC<br>Leu Phe Ile Glu Gly Leu Tyr Leu Phe Thr Leu Leu Val Glu Thr Phe<br>305 310 315     | 1021 |     |  |
| TTC CCT GAA AGG AGA TAC TTC TAC TGG TAC ACC ATC ATT GGC TGG GGG<br>Phe Pro Glu Arg Arg Tyr Phe Tyr Trp Tyr Thr Ile Ile Gly Trp Gly<br>320 325 330     | 1069 |     |  |
| TCC CCA ACT GTG TGT GTG ACA GTG TGG GCT ACG CTG AGA CTC TAC TTT<br>Ser Pro Thr Val Cys Val Thr Val Trp Ala Thr Leu Arg Leu Tyr Phe<br>335 340 345     | 1117 |     |  |
| GAT GAC ACA GGC TGC TGG GAT ATG AAT GAC AGC ACA GCT CTG TGG TGG<br>Asp Asp Thr Gly Cys Trp Asp Met Asn Asp Ser Thr Ala Leu Trp Trp<br>350 355 360     | 1165 |     |  |
| GTG ATC AAA GGC CCT GTG GTT GGC TCT ATC ATG GTT AAC TTT GTG CTT<br>Val Ile Lys Gly Pro Val Val Gly Ser Ile Met Val Asn Phe Val Leu<br>365 370 375 380 | 1213 |     |  |
| TTT ATT GGC ATT ATC GTC ATC CTT GTG CAG AAA CTT CAG TCT CCA GAC<br>Phe Ile Gly Ile Ile Val Ile Leu Val Gln Lys Leu Gln Ser Pro Asp<br>385 390 395     | 1261 |     |  |
| ATG GGA GGC AAT GAG TCC AGC ATC TAC TTG CGA CTG GCC CGG TCC ACC<br>Met Gly Gly Asn Glu Ser Ser Ile Tyr Leu Arg Leu Ala Arg Ser Thr<br>400 405 410     | 1309 |     |  |

FIG. 13B

|     |            |         |     |     |     |     |     |     |     |     |     |     |     |     |     |      |
|-----|------------|---------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| CTG | CTG        | CTC     | ATC | CCA | CTA | TTC | GGA | ATC | CAC | TAC | ACA | GTA | TTT | GCC | TTC | 1357 |
| Leu | Leu        | Leu     | Ile | Pro | Leu | Phe | Gly | Ile | His | Tyr | Thr | Val | Phe | Ala | Phe |      |
|     |            | 415     |     |     |     |     | 420 |     |     |     |     | 425 |     |     |     |      |
| TCC | CCA        | GAG     | AAT | GTC | AGC | AAA | AGG | GAA | AGA | CTC | GTG | TTT | GAG | CTG | GGG | 1405 |
| Ser | Pro        | Glu     | Asn | Val | Ser | Lys | Arg | Glu | Arg | Leu | Val | Phe | Glu | Leu | Gly |      |
|     | 430        |         |     |     |     | 435 |     |     |     |     | 440 |     |     |     |     |      |
| CTG | GGC        | TCC     | TTC | CAG | GGC | TTT | GTG | GTG | GCT | GTT | CTC | TAC | TGT | TTT | CTG | 1453 |
| Leu | Gly        | Ser     | Phe | Gln | Gly | Phe | Val | Val | Ala | Val | Leu | Tyr | Cys | Phe | Leu |      |
| 445 |            |         |     |     | 450 |     |     |     |     | 455 |     |     |     |     | 460 |      |
| AAT | GGT        | GAG     | GTA | CAA | GCG | GAG | ATC | AAG | CGA | AAA | TGG | CGA | AGC | TGG | AAG | 1501 |
| Asn | Gly        | Glu     | Val | Gln | Ala | Glu | Ile | Lys | Arg | Lys | Trp | Arg | Ser | Trp | Lys |      |
|     |            |         |     | 465 |     |     |     |     | 470 |     |     |     |     | 475 |     |      |
| GTG | AAC        | CGT     | TAC | TTC | GCT | GTG | GAC | TTC | AAG | CAC | CGA | CAC | CCG | TCT | CTG | 1549 |
| Val | Asn        | Arg     | Tyr | Phe | Ala | Val | Asp | Phe | Lys | His | Arg | His | Pro | Ser | Leu |      |
|     |            |         | 480 |     |     |     |     | 485 |     |     |     |     | 490 |     |     |      |
| GCC | AGC        | AGT     | GGG | GTG | AAT | GGG | GGC | ACC | CAG | CTC | TCC | ATC | CTG | AGC | AAG | 1597 |
| Ala | Ser        | Ser     | Gly | Val | Asn | Gly | Gly | Thr | Gln | Leu | Ser | Ile | Leu | Ser | Lys |      |
|     |            | 495     |     |     |     |     | 500 |     |     |     |     | 505 |     |     |     |      |
| AGC | AGC        | TCC     | CAA | ATC | CGC | ATG | TCT | GGC | CTC | CCT | GCT | GAC | AAT | CTG | GCC | 1645 |
| Ser | Ser        | Ser     | Gln | Ile | Arg | Met | Ser | Gly | Leu | Pro | Ala | Asp | Asn | Leu | Ala |      |
|     | 510        |         |     |     |     | 515 |     |     |     |     | 520 |     |     |     |     |      |
| ACC | TGAGCCATGC | TCCCCCT |     |     |     |     |     |     |     |     |     |     |     |     |     | 1664 |
| Thr |            |         |     |     |     |     |     |     |     |     |     |     |     |     |     |      |
| 525 |            |         |     |     |     |     |     |     |     |     |     |     |     |     |     |      |

FIG. 13C

Rat  
Type I-B      Asn Glu Ser Ser Ile Tyr Phe Ser Cys Val Gln Lys Cys Tyr Cys Lys  
AAC GAG TCC AGC ATC TAC TTC AGC TGC GTG CAG AAA TGC TAC TGC AAA

pHRP15A  
human Type I-B      Asn Glu Ser Ser Ile Tyr Phe Ser Cys Val Gln Lys Cys Tyr Cys Lys  
AAT GAG TCC AGC ATC TAC TTC AGC TGC GTG CAG AAA TGC TAC TGC AAG

pHRP55A  
Type I-B2      Asn Glu Ser Ser Ile Tyr Phe — Cys Val Gln Lys Cys Tyr Cys Lys  
AAT GAG TCC AGC ATC TAC TTC TGC GTG CAG AAA TGC TAC TGC AAG

pHRP66P  
Type I-C      Asn Glu Ser Ser Ile Tyr Leu Thr Asn Leu Ser Pro Arg Val Pro Lys  
AAT GAG TCC AGC ATC TAC TTA ACA AAT TTA AGC CCG CGA GTC CCC AAG

Pro Gln Arg Ala Gln Gln His Ser Cys Lys Met Ser Glu Leu Ser Thr  
CCA CAG CGG CGT CAG CAG CAC TCT TGC AAG ATC TCA GAA CTA TCC ACC

Pro Gln Arg Ala Gln Gln His Ser Cys Lys Met Ser Glu Leu Ser Thr  
CCA CAG CGG GCT CAG CAG CAC TCT TGC AAG ATG TCA GAA CTG TCC ACC

Pro Gln Arg Ala Gln Gln His Ser Cys Lys Met Ser Glu Leu Ser Thr  
CCA CAG CGG GCT CAG CAG CAC TCT TGC AAG ATG TCA GAA CTG TCC ACC

Lys Ala Arg Glu Asp Pro Leu Pro Val Pro Ser Asp Gln His Ser Leu  
AAA GCC CGA GAG GAC CCC CTG CCT GTG CCC TCA GAC CAG CAT TCA CTC

Ile Thr Leu Arg Leu Ala Arg Ser Thr Leu  
ATT ACT CTA CGG CTG GCC CGC TCC ACC CTA

Ile Thr Leu Arg Leu Ala Arg Ser Thr Leu  
ATT ACT CTG CGA CTG GCC CGG TCC ACC CTG

Ile Thr Leu Arg Leu Ala Arg Ser Thr Leu  
ATT ACT CTG CGA CTG GCC CGG TCC ACC CTG

Pro Phe Leu Arg Leu Ala Arg Ser Thr Leu  
CCT TTC CTG CGA CTG GCC CGG TCC ACC CTG

FIG. 15

|   |     |
|---|-----|
| AGCCCAGAGA CACATTGGGG CTGACCTGCC GCTGCTGTCA GTGGGAGGCC AGTGGTGCTG | 60  |
| GCCAAGAAAGT GTC ATG GCT GGT GTC GTG CAC GTT TCC CTG GCT GCT CAC   | 109 |
| Met Ala Gly Val Val His Val Ser Leu Ala Ala His                   |     |
| 1 5 10  |     |
| TGC GGG GCC TGT CCG TGG GGC CGG GGC AGA CTC CGC AAA GGA CGC GCA   | 157 |
| Cys Gly Ala Cys Pro Trp Gly Arg Gly Arg Leu Arg Lys Gly Arg Ala   |     |
| 15 20 25  |     |
| GCC TGC AAG TCC GCG GCC CAG AGA CAC ATT GGG GCT GAC CTG CCG CTG   | 205 |
| Ala Cys Lys Ser Ala Ala Gln Arg His Ile Gly Ala Asp Leu Pro Leu   |     |
| 30 35 40  |     |
| CTG TCA GTG GGA GGC CAG TGG TGC TGG CCA AGA AGT GTC ATG GCT GGT   | 253 |
| Leu Ser Val Gly Gly Gln Trp Cys Trp Pro Arg Ser Val Met Ala Gly   |     |
| 45 50 55 60   |     |
| GTC GTG CAC GTT TCC CTG GCT GCT CTC CTC CTG CTG CCT ATG GCC CCT   | 301 |
| Val Val His Val Ser Leu Ala Ala Leu Leu Leu Leu Pro Met Ala Pro   |     |
| 65 70 75  |     |
| GCC ATG CAT TCT GAC TGC ATC TTC AAG AAG GAG CAA GCC ATG TGC CTG   | 349 |
| Ala Met His Ser Asp Cys Ile Phe Lys Lys Glu Gln Ala Met Cys Leu   |     |
| 80 85 90  |     |
| GAG AAG ATC CAG AGG GCC AAT GAG CTG ATG GGC TTC AAT GAT TCC TCT   | 397 |
| Glu Lys Ile Gln Arg Ala Asn Glu Leu Met Gly Phe Asn Asp Ser Ser   |     |
| 95 100 105  |     |
| CCA GGC TGT CCT GGG ATG TGG GAC AAC ATC ACG TGT TGG AAG CCC GCC   | 445 |
| Pro Gly Cys Pro Gly Met Trp Asp Asn Ile Thr Cys Trp Lys Pro Ala   |     |
| 110 115 120   |     |
| CAT GTG GGT GAG ATG GTC CTG GTC AGC TGC CCT GAG CTC TTC CGA ATC   | 493 |
| His Val Gly Glu Met Val Leu Val Ser Cys Pro Glu Leu Phe Arg Ile   |     |
| 125 130 135 140   |     |
| TTC AAC CCA GAC CAA GTC TGG GAG ACC GAA ACC ATT GGA GAG TCT GAT   | 541 |
| Phe Asn Pro Asp Gln Val Trp Glu Thr Glu Thr Ile Gly Glu Ser Asp   |     |
| 145 150 155   |     |
| TTT GGT GAC AGT AAC TCC TTA GAT CTC TCA GAC ATG GGA GTG GTG AGC   | 589 |
| Phe Gly Asp Ser Asn Ser Leu Asp Leu Ser Asp Met Gly Val Val Ser   |     |
| 160 165 170   |     |
| CGG AAC TGC ACG GAG GAT GGC TGG TCG GAA CCC TTC CCT CAT TAC TTT   | 637 |
| Arg Asn Cys Thr Glu Asp Gly Trp Ser Glu Pro Phe Pro His Tyr Phe   |     |
| 175 180 185   |     |
| GAT GCC TGT GGG TTT GAT GAA TAT GAA TCT GAG ACT GGG GAC CAG GAT   | 685 |
| Asp Ala Cys Gly Phe Asp Glu Tyr Glu Ser Glu Thr Gly Asp Gln Asp   |     |

FIG. 16A



TAC TGC AAG CCA CAG CGG GCT CAG CAG CAC TCT TGC AAG ATG TCA GAA 1357  
 Tyr Cys Lys Pro Gln Arg Ala Gln Gln His Ser Cys Lys Met Ser Glu  
 415 420 425

CTG TCC ACC ATT ACT CTG CGA CTG GCC CGG TCC ACC CTG CTG CTC ATC 1405  
 Leu Ser Thr Ile Thr Leu Arg Leu, Ala Arg Ser Thr Leu Leu Leu Ile  
 430 435 440

CCA CTA TTC GGA ATC CAC TAC ACA GTA TTT GCC TTC TCC CCA GAG AAT 1453  
 Pro Leu Phe Gly Ile His Tyr Thr Val Phe Ala Phe Ser Pro Glu Asn  
 445 450 455 460

GTC AGC AAA AGG GAA AGA CTC GTG TTT GAG CTG GGG CTG GGC TCC TTC 1501  
 Val Ser Lys Arg Glu Arg Leu Val Phe Glu Leu Gly Leu Gly Ser Phe  
 465 470 475

CAG GGC TTT GTG GTG GCT GTT CTC TAC TGT TTT CTG AAT GGT GAG GTA 1549  
 Gln Gly Phe Val Val Ala Val Leu Tyr Cys Phe Leu Asn Gly Glu Val  
 480 485 490

CAA GCG GAG ATC AAG CGA AAA TGG CGA AGC TGG AAG GTG AAC CGT TAC 1597  
 Gln Ala Glu Ile Lys Arg Lys Trp Arg Ser Trp Lys Val Asn Arg Tyr  
 495 500 505

TTC GCT GTG GAC TTC AAG CAC CGA CAC CCG TCT CTG GCC AGC AGT GGG 1645  
 Phe Ala Val Asp Phe Lys His Arg His Pro Ser Leu Ala Ser Ser Gly  
 510 515 520

GTG AAT GGG GGC ACC CAG CTC TCC ATC CTG AGC AAG AGC AGC TCC CAA 1693  
 Val Asn Gly Gly Thr Gln Leu Ser Ile Leu Ser Lys Ser Ser Ser Gln  
 525 530 535 540

ATC CGC ATG TCT GGC CTC CCT GCT GAC AAT CTG GCC ACC TGAGCCATGC TCC 1745  
 Ile Arg Met Ser Gly Leu Pro Ala Asp Asn Leu Ala Thr  
 545 550

CCT 1748

FIG. 16C

|   |     |
|---|-----|
| AGCCCAGAGA CACATTGGGG CTGACCTGCC GCTGCTGTCA GTGGGAGGCC AGTGGTGCTG | 60  |
| GCCAAGAAGT GTC ATG GCT GGT GTC GTG CAC GTT TCC CTG GCT GCT CAC    | 109 |
| Met Ala Gly Val Val His Val Ser Leu Ala Ala His                   |     |
| 1 5 10  |     |
| TGC GGG GCC TGT CCG TGG GGC CGG GGC AGA CTC CGC AAA GGA CGC GCA   | 157 |
| Cys Gly Ala Cys Pro Trp Gly Arg Gly Arg Leu Arg Lys Gly Arg Ala   |     |
| 15 20 25  |     |
| GCC TGC AAG TCC GCG GCC CAG AGA CAC ATT GGG GCT GAC CTG CCG CTG   | 205 |
| Ala Cys Lys Ser Ala Ala Gln Arg His Ile Gly Ala Asp Leu Pro Leu   |     |
| 30 35 40  |     |
| CTG TCA GTG GGA GGC CAG TGG TGC TGG CCA AGA AGT GTC ATG GCT GGT   | 253 |
| Leu Ser Val Gly Gly Gln Trp Cys Trp Pro Arg Ser Val Met Ala Gly   |     |
| 45 50 55 60   |     |
| GTC GTG CAC GTT TCC CTG GCT GCT CTC CTC CTG CTG CCT ATG GCC CCT   | 301 |
| Val Val His Val Ser Leu Ala Ala Leu Leu Leu Leu Pro Met Ala Pro   |     |
| 65 70 75  |     |
| GCC ATG CAT TCT GAC TGC ATC TTC AAG AAG GAG CAA GCC ATG TGC CTG   | 349 |
| Ala Met His Ser Asp Cys Ile Phe Lys Lys Glu Gln Ala Met Cys Leu   |     |
| 80 85 90  |     |
| GAG AAG ATC CAG AGG GCC AAT GAG CTG ATG GGC TTC AAT GAT TCC TCT   | 397 |
| Glu Lys Ile Gln Arg Ala Asn Glu Leu Met Gly Phe Asn Asp Ser Ser   |     |
| 95 100 105  |     |
| CCA GGC TGT CCT GGG ATG TGG GAC AAC ATC ACG TGT TGG AAG CCC GCC   | 445 |
| Pro Gly Cys Pro Gly Met Trp Asp Asn Ile Thr Cys Trp Lys Pro Ala   |     |
| 110 115 120   |     |
| CAT GTG GGT GAG ATG GTC CTG GTC AGC TGC CCT GAG CTC TTC CGA ATC   | 493 |
| His Val Gly Glu Met Val Leu Val Ser Cys Pro Glu Leu Phe Arg Ile   |     |
| 125 130 135 140   |     |
| TTC AAC CCA GAC CAA GTC TGG GAG ACC GAA ACC ATT GGA GAG TCT GAT   | 541 |
| Phe Asn Pro Asp Gln Val Trp Glu Thr Glu Thr Ile Gly Glu Ser Asp   |     |
| 145 150 155   |     |
| TTT GGT GAC AGT AAC TCC TTA GAT CTC TCA GAC ATG GGA GTG GTG AGC   | 589 |
| Phe Gly Asp Ser Asn Ser Leu Asp Leu Ser Asp Met Gly Val Val Ser   |     |
| 160 165 170   |     |
| CGG AAC TGC ACG GAG GAT GGC TGG TCG GAA CCC TTC CCT CAT TAC TTT   | 637 |
| Arg Asn Cys Thr Glu Asp Gly Trp Ser Glu Pro Phe Pro His Tyr Phe   |     |
| 175 180 185   |     |
| GAT GCC TGT GGG TTT GAT GAA TAT GAA TCT GAG ACT GGG GAC CAG GAT   | 685 |
| Asp Ala Cys Gly Phe Asp Glu Tyr Glu Ser Glu Thr Gly Asp Gln Asp   |     |
| 190 195 200   |     |

FIG. 17A

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |      |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| TAT | TAC | TAC | CTG | TCA | GTG | AAG | GCC | CTC | TAC | ACG | GTT | GGC | TAC | AGC | ACA | 733  |
| Tyr | Tyr | Tyr | Leu | Ser | Val | Lys | Ala | Leu | Tyr | Thr | Val | Gly | Tyr | Ser | Thr |      |
| 205 |     |     |     |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |      |
| TCC | CTC | GTC | ACC | CTC | ACC | ACT | GCC | ATG | GTC | ATC | CTT | TGT | CGC | TTC | CGG | 781  |
| Ser | Leu | Val | Thr | Leu | Thr | Thr | Ala | Met | Val | Ile | Leu | Cys | Arg | Phe | Arg |      |
|     |     |     |     | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |      |
| AAG | CTG | CAC | TGC | ACA | CGC | AAC | TTC | ATC | CAC | ATG | AAC | CTG | TTT | GTG | TCG | 829  |
| Lys | Leu | His | Cys | Thr | Arg | Asn | Phe | Ile | His | Met | Asn | Leu | Phe | Val | Ser |      |
|     |     |     | 240 |     |     |     |     | 245 |     |     |     |     | 250 |     |     |      |
| TTC | ATG | CTG | AGG | GCG | ATC | TCC | GTC | TTC | ATC | AAA | GAC | TGG | ATT | CTG | TAT | 877  |
| Phe | Met | Leu | Arg | Ala | Ile | Ser | Val | Phe | Ile | Lys | Asp | Trp | Ile | Leu | Tyr |      |
|     |     | 255 |     |     |     |     | 260 |     |     |     |     | 265 |     |     |     |      |
| GCG | GAG | CAG | GAC | AGC | AAC | CAC | TGC | TTC | ATC | TCC | ACT | GTG | GAA | TGT | AAG | 925  |
| Ala | Glu | Gln | Asp | Ser | Asn | His | Cys | Phe | Ile | Ser | Thr | Val | Glu | Cys | Lys |      |
|     | 270 |     |     |     |     | 275 |     |     |     |     | 280 |     |     |     |     |      |
| GCC | GTC | ATG | GTT | TTC | TTC | CAC | TAC | TGT | GTT | GTG | TCC | AAC | TAC | TTC | TGG | 973  |
| Ala | Val | Met | Val | Phe | Phe | His | Tyr | Cys | Val | Val | Ser | Asn | Tyr | Phe | Trp |      |
| 285 |     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |      |
| CTG | TTC | ATC | GAG | GGC | CTG | TAC | CTC | TTC | ACT | CTG | CTG | GTG | GAG | ACC | TTC | 1021 |
| Leu | Phe | Ile | Glu | Gly | Leu | Tyr | Leu | Phe | Thr | Leu | Leu | Val | Glu | Thr | Phe |      |
|     |     |     |     | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |      |
| TTC | CCT | GAA | AGG | AGA | TAC | TTC | TAC | TGG | TAC | ACC | ATC | ATT | GGC | TGG | GGG | 1069 |
| Phe | Pro | Glu | Arg | Arg | Tyr | Phe | Tyr | Trp | Tyr | Thr | Ile | Ile | Gly | Trp | Gly |      |
|     |     |     | 320 |     |     |     |     | 325 |     |     |     |     | 330 |     |     |      |
| ACC | CCA | ACT | GTG | TGT | GTG | ACA | GTG | TGG | GCT | ACG | CTG | AGA | CTC | TAC | TTT | 1117 |
| Thr | Pro | Thr | Val | Cys | Val | Thr | Val | Trp | Ala | Thr | Leu | Arg | Leu | Tyr | Phe |      |
|     |     |     | 335 |     |     |     | 340 |     |     |     |     | 345 |     |     |     |      |
| GAT | GAC | ACA | GGC | TGC | TGG | GAT | ATG | AAT | GAC | AGC | ACA | GCT | CTG | TGG | TGG | 1165 |
| Asp | Asp | Thr | Gly | Cys | Trp | Asp | Met | Asn | Asp | Ser | Thr | Ala | Leu | Trp | Trp |      |
|     |     | 350 |     |     |     | 355 |     |     |     |     | 360 |     |     |     |     |      |
| GTG | ATC | AAA | GGC | CCT | GTG | GTT | GGC | TCT | ATC | ATG | GTT | AAC | TTT | GTG | CTT | 1213 |
| Val | Ile | Lys | Gly | Pro | Val | Val | Gly | Ser | Ile | Met | Val | Asn | Phe | Val | Leu |      |
| 365 |     |     |     |     | 370 |     |     |     |     | 375 |     |     |     | 380 |     |      |
| TTT | ATT | GGC | ATT | ATC | GTC | ATC | CTT | GTG | CAG | AAA | CTT | CAG | TCT | CCA | GAC | 1261 |
| Phe | Ile | Gly | Ile | Ile | Val | Ile | Leu | Val | Gln | Lys | Leu | Gln | Ser | Pro | Asp |      |
|     |     |     |     | 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |      |
| ATG | GGA | GGC | AAT | GAG | TCC | AGC | ATC | TAC | TTC | TGC | GTG | CAG | AAA | TGC | TAC | 1309 |
| Met | Gly | Gly | Asn | Glu | Ser | Ser | Ile | Tyr | Phe | Cys | Val | Gln | Lys | Cys | Tyr |      |
|     |     |     | 400 |     |     |     | 405 |     |     |     |     | 410 |     |     |     |      |
| TGC | AAG | CCA | CAG | CGG | GCT | CAG | CAG | CAC | TCT | TGC | AAG | ATG | TCA | GAA | CTG | 1357 |
| Cys | Lys | Pro | Gln | Arg | Ala | Gln | Gln | His | Ser | Cys | Lys | Met | Ser | Glu | Leu |      |

FIG. 17B



| 415   | 420 | 425 |      |
|---|-----|-----|------|
| TCC ACC ATT ACT CTG CGA CTG GCC CGG TCC ACC CTG CTG CTC ATC CCA<br>Ser Thr Ile Thr Leu Arg Leu Ala Arg Ser Thr Leu Leu Leu Ile Pro<br>430 435 440     |     |     | 1405 |
| CTA TTC GGA ATC CAC TAC ACA GTA TTT GCC TTC TCC CCA GAG AAT GTC<br>Leu Phe Gly Ile His Tyr Thr Val Phe Ala Phe Ser Pro Glu Asn Val<br>445 450 455 460 |     |     | 1453 |
| AGC AAA AGG GAA AGA CTC GTG TTT GAG CTG GGG CTG GGC TCC TTC CAG<br>Ser Lys Arg Glu Arg Leu Val Phe Glu Leu Gly Leu Gly Ser Phe Gln<br>465 470 475     |     |     | 1501 |
| GGC TTT GTG GTG GCT GTT CTC TAC TGT TTT CTG AAT GGT GAG GTA CAA<br>Gly Phe Val Val Ala Val Leu Tyr Cys Phe Leu Asn Gly Glu Val Gln<br>480 485 490     |     |     | 1549 |
| GCG GAG ATC AAG CGA AAA TGG CGA AGC TGG AAG GTG AAC CGT TAC TTC<br>Ala Glu Ile Lys Arg Lys Trp Arg Ser Trp Lys Val Asn Arg Tyr Phe<br>495 500 505     |     |     | 1597 |
| GCT GTG GAC TTC AAG CAC CGA CAC CCG TCT CTG GCC AGC AGT GGG GTG<br>Ala Val Asp Phe Lys His Arg His Pro Ser Leu Ala Ser Ser Gly Val<br>510 515 520     |     |     | 1645 |
| AAT GGG GGC ACC CAG CTC TCC ATC CTG AGC AAG AGC AGC TCC CAA ATC<br>Asn Gly Gly Thr Gln Leu Ser Ile Leu Ser Lys Ser Ser Ser Gln Ile<br>525 530 535 540 |     |     | 1693 |
| CGC ATG TCT GGC CTC CCT GCT GAC AAT CTG GCC ACC TGAGCCATGC TCCCCT<br>Arg Met Ser Gly Leu Pro Ala Asp Asn Leu Ala Thr ***<br>545 550                   |     |     | 1745 |

FIG. 17C

|   |     |
|---|-----|
| AGCCCAGAGA CACATTGGGG CTGACCTGCC GCTGCTGTCA GTGGGAGGCC AGTGGTGCTG | 60  |
| GCCAAGAAGT GTC ATG GCT GGT GTC GTG CAC GTT TCC CTG GCT GCT CAC    | 109 |
| Met Ala Gly Val Val His Val Ser Leu Ala Ala His                   |     |
| 1 5 10  |     |
| TGC GGG GCC TGT CCG TGG GGC CGG GGC AGA CTC CGC AAA GGA CGC GCA   | 157 |
| Cys Gly Ala Cys Pro Trp Gly Arg Gly Arg Leu Arg Lys Gly Arg Ala   |     |
| 15 20 25  |     |
| GCC TGC AAG TCC GCG GCC CAG AGA CAC ATT GGG GCT GAC CTG CCG CTG   | 205 |
| Ala Cys Lys Ser Ala Ala Gln Arg His Ile Gly Ala Asp Leu Pro Leu   |     |
| 30 35 40  |     |
| CTG TCA GTG GGA GGC CAG TGG TGC TGG CCA AGA AGT GTC ATG GCT GGT   | 253 |
| Leu Ser Val Gly Gly Gln Trp Cys Trp Pro Arg Ser Val Met Ala Gly   |     |
| 45 50 55 60   |     |
| GTC GTG CAC GTT TCC CTG GCT GCT CTC CTC CTG CTG CCT ATG GCC CCT   | 301 |
| Val Val His Val Ser Leu Ala Ala Leu Leu Leu Leu Pro Met Ala Pro   |     |
| 65 70 75  |     |
| GCC ATG CAT TCT GAC TGC ATC TTC AAG AAG GAG CAA GCC ATG TGC CTG   | 349 |
| Ala Met His Ser Asp Cys Ile Phe Lys Lys Glu Gln Ala Met Cys Leu   |     |
| 80 85 90  |     |
| GAG AAG ATC CAG AGG GCC AAT GAG CTG ATG GGC TTC AAT GAT TCC TCT   | 397 |
| Glu Lys Ile Gln Arg Ala Asn Glu Leu Met Gly Phe Asn Asp Ser Ser   |     |
| 95 100 105  |     |
| CCA GGC TGT CCT GGG ATG TGG GAC AAC ATC ACG TGT TGG AAG CCC GCC   | 445 |
| Pro Gly Cys Pro Gly Met Trp Asp Asn Ile Thr Cys Trp Lys Pro Ala   |     |
| 110 115 120   |     |
| CAT GTG GGT GAG ATG GTC CTG GTC AGC TGC CCT GAG CTC TTC CGA ATC   | 493 |
| His Val Gly Glu Met Val Leu Val Ser Cys Pro Glu Leu Phe Arg Ile   |     |
| 125 130 135 140   |     |
| TTC AAC CCA GAC CAA GTC TGG GAG ACC GAA ACC ATT GGA GAG TCT GAT   | 541 |
| Phe Asn Pro Asp Gln Val Trp Glu Thr Glu Thr Ile Gly Glu Ser Asp   |     |
| 145 150 155   |     |
| TTT GGT GAC AGT AAC TCC TTA GAT CTC TCA GAC ATG GGA GTG GTG AGC   | 589 |
| Phe Gly Asp Ser Asn Ser Leu Asp Leu Ser Asp Met Gly Val Val Ser   |     |
| 160 165 170   |     |
| CGG AAC TGC ACG GAG GAT GGC TGG TCG GAA CCC TTC CCT CAT TAC TTT   | 637 |
| Arg Asn Cys Thr Glu Asp Gly Trp Ser Glu Pro Phe Pro His Tyr Phe   |     |
| 175 180 185   |     |
| GAT GCC TGT GGG TTT GAT GAA TAT GAA TCT GAG ACT GGG GAC CAG GAT   | 685 |
| Asp Ala Cys Gly Phe Asp Glu Tyr Glu Ser Glu Thr Gly Asp Gln Asp   |     |

FIG. 18A

| 190   | 195 | 200 |      |
|---|-----|-----|------|
| TAT TAC TAC CTG TCA GTG AAG GCC CTC TAC ACG GTT GGC TAC AGC ACA<br>Tyr Tyr Tyr Leu Ser Val Lys Ala Leu Tyr Thr Val Gly Tyr Ser Thr<br>205 210 215 220 |     |     | 733  |
| TCC CTC GTC ACC CTC ACC ACT GCC ATG GTC ATC CTT TGT CGC TTC CGG<br>Ser Leu Val Thr Leu Thr Thr Ala Met Val Ile Leu Cys Arg Phe Arg<br>225 230 235     |     |     | 781  |
| AAG CTG CAC TGC ACA CGC AAC TTC ATC CAC ATG AAC CTG TTT GTG TCG<br>Lys Leu His Cys Thr Arg Asn Phe Ile His Met Asn Leu Phe Val Ser<br>240 245 250     |     |     | 829  |
| TTC ATG CTG AGG GCG ATC TCC GTC TTC ATC AAA GAC TGG ATT CTG TAT<br>Phe Met Leu Arg Ala Ile Ser Val Phe Ile Lys Asp Trp Ile Leu Tyr<br>255 260 265     |     |     | 877  |
| GCG GAG CAG GAC AGC AAC CAC TGC TTC ATC TCC ACT GTG GAA TGT AAG<br>Ala Glu Gln Asp Ser Asn His Cys Phe Ile Ser Thr Val Glu Cys Lys<br>270 275 280     |     |     | 925  |
| GCC GTC ATG GTT TTC TTC CAC TAC TGT GTT GTG TCC AAC TAC TTC TGG<br>Ala Val Met Val Phe Phe His Tyr Cys Val Val Ser Asn Tyr Phe Trp<br>285 290 295 300 |     |     | 973  |
| CTG TTC ATC GAG GGC CTG TAC CTC TTC ACT CTG CTG GTG GAG ACC TTC<br>Leu Phe Ile Glu Gly Leu Tyr Leu Phe Thr Leu Leu Val Glu Thr Phe<br>305 310 315     |     |     | 1021 |
| TTC CCT GAA AGG AGA TAC TTC TAC TGG TAC ACC ATC ATT GGC TGG GGG<br>Phe Pro Glu Arg Arg Tyr Phe Tyr Trp Tyr Thr Ile Ile Gly Trp Gly<br>320 325 330     |     |     | 1069 |
| ACC CCA ACT GTG TGT GTG ACA GTG TGG GCT ACG CTG AGA CTC TAC TTT<br>Thr Pro Thr Val Cys Val Thr Val Trp Ala Thr Leu Arg Leu Tyr Phe<br>335 340 345     |     |     | 1117 |
| GAT GAC ACA GGC TGC TGG GAT ATG AAT GAC AGC ACA GCT CTG TGG TGG<br>Asp Asp Thr Gly Cys Trp Asp Met Asn Asp Ser Thr Ala Leu Trp Trp<br>350 355 360     |     |     | 1165 |
| GTG ATC AAA GGC CCT GTG GTT GGC TCT ATC ATG GTT AAC TTT GTG CTT<br>Val Ile Lys Gly Pro Val Val Gly Ser Ile Met Val Asn Phe Val Leu<br>365 370 375 380 |     |     | 1213 |
| TTT ATT GGC ATT ATC GTC ATC CTT GTG CAG AAA CTT CAG TCT CCA GAC<br>Phe Ile Gly Ile Ile Val Ile Leu Val Gln Lys Leu Gln Ser Pro Asp<br>385 390 395     |     |     | 1261 |
| ATG GGA GGC AAT GAG TCC AGC ATC TAC TTA ACA AAT TTA AGC CCG CGA<br>Met Gly Gly Asn Glu Ser Ser Ile Tyr Leu Thr Asn Leu Ser Pro Arg<br>400 405 410     |     |     | 1309 |

FIG. 18B

|  |      |
|--|------|
| GTC CCC AAG AAA GCC CGA GAG GAC CCC CTG CCT GTG CCC TCA GAC CAG    | 1357 |
| Val Pro Lys Lys Ala Arg Glu Asp Pro Leu Pro Val Pro Ser Asp Gln    |      |
| 415 420 425  |      |
| CAT TCA CTC CCT TTC CTG CGA CTG GCC CGG TCC ACC CTG CTG CTC ATC    | 1405 |
| His Ser Leu Pro Phe Leu Arg Leu Ala Arg Ser Thr Leu Leu Leu Ile    |      |
| 430 435 440  |      |
| CCA CTA TTC GGA ATC CAC TAC ACA GTA TTT GCC TTC TCC CCA GAG AAT    | 1453 |
| Pro Leu Phe Gly Ile His Tyr Thr Val Phe Ala Phe Ser Pro Glu Asn    |      |
| 445 450 455 460  |      |
| GTC AGC AAA AGG GAA AGA CTC GTG TTT GAG CTG GGG CTG GGC TCC TTC    | 1501 |
| Val Ser Lys Arg Glu Arg Leu Val Phe Glu Leu Gly Leu Gly Ser Phe    |      |
| 465 470 475  |      |
| CAG GGC TTT GTG GTG GCT GTT CTC TAC TGT TTT CTG AAT GGT GAG GTA    | 1549 |
| Gln Gly Phe Val Val Ala Val Leu Tyr Cys Phe Leu Asn Gly Glu Val    |      |
| 480 485 490  |      |
| CAA GCG GAG ATC AAG CGA AAA TGG CGA AGC TGG AAG GTG AAC CGT TAC    | 1597 |
| Gln Ala Glu Ile Lys Arg Lys Trp Arg Ser Trp Lys Val Asn Arg Tyr    |      |
| 495 500 505  |      |
| TTC GCT GTG GAC TTC AAG CAC CGA CAC CCG TCT CTG GCC AGC AGT GGG    | 1645 |
| Phe Ala Val Asp Phe Lys His Arg His Pro Ser Leu Ala Ser Ser Gly    |      |
| 510 515 520  |      |
| GTG AAT GGG GGC ACC CAG CTC TCC ATC CTG AGC AAG AGC AGC TCC CAA    | 1693 |
| Val Asn Gly Gly Thr Gln Leu Ser Ile Leu Ser Lys Ser Ser Ser Gln    |      |
| 525 530 535 540  |      |
| ATC CGC ATG TCT GGC CTC CCT GCT GAC AAT CTG GCC ACC TGAGCCATGC TCC | 1745 |
| Ile Arg Met Ser Gly Leu Pro Ala Asp Asn Leu Ala Thr ***            |      |
| 545 550  |      |
| CCT  | 1748 |

FIG. 18C

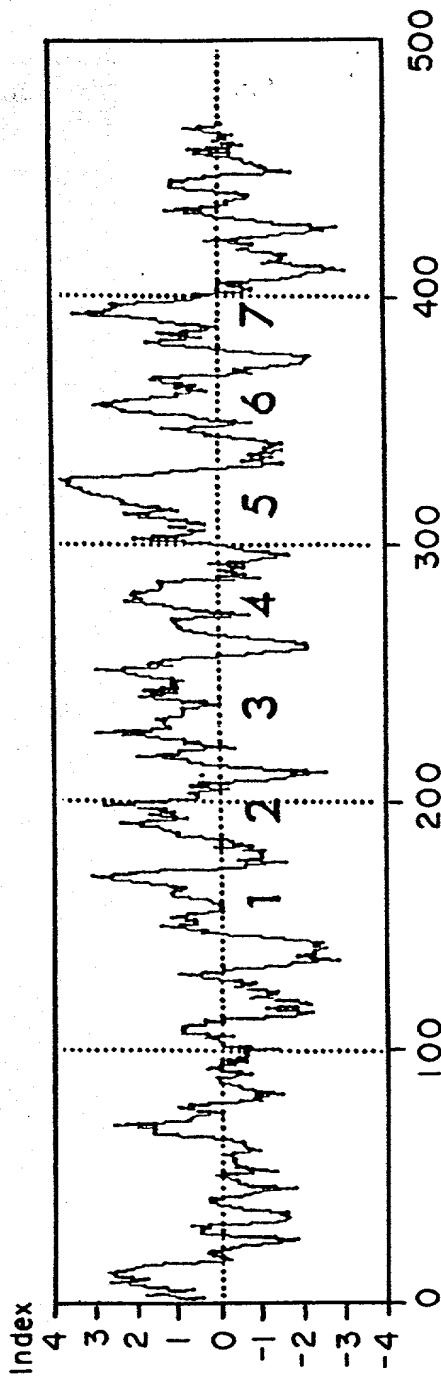


FIG. 19A

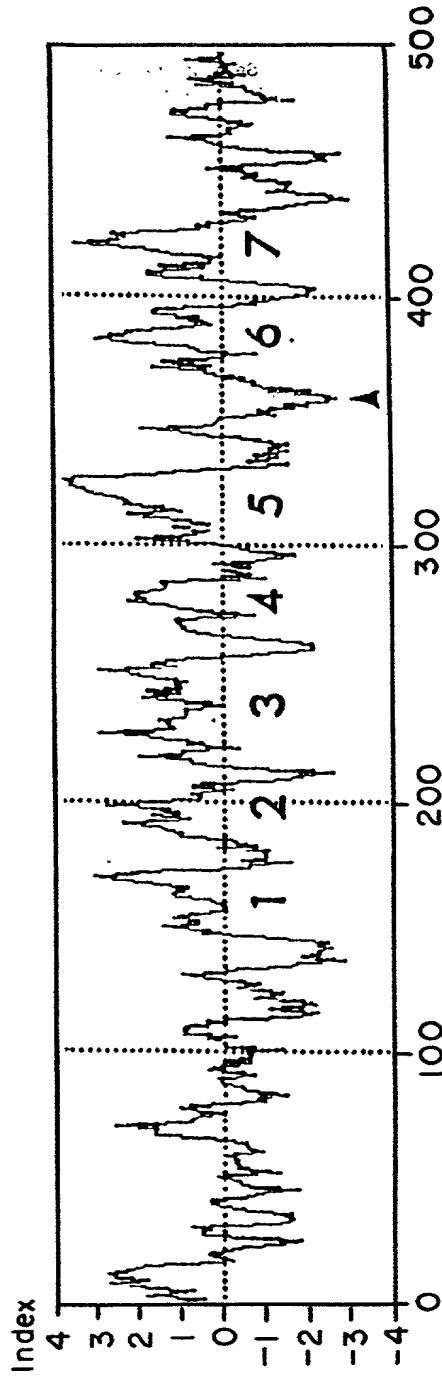


FIG. 19B

|  |       |       |       |       |       |       |
|--|-------|-------|-------|-------|-------|-------|
| 19   | 29    | 39    | 49    | 59    | 69    | 79    |
| TALLLPVAIAMHSDCIFKKEQAMCLERIQRANDLMGLNESSPGCPGMWDNITCWKPAQVGEMVLVSCPEV |       |       |       |       |       |       |
| *  | *     | **    | *     | *     | *     | **    |
| MRPPSPPHVRWLCVLAGALACALRPAGSQAASPOHECEYLQLEIQRQQCLEEAQLENETTGCCKMWDNL  |       |       |       |       |       |       |
| 10   | 20    | 30    | 40    | 50    | 60    | 70    |
|  |       |       |       |       |       |       |
| 89   | 99    | 109   | 119   | 129   | 139   | 149   |
| FRIFNPQVWMTETIGDSGFADSNSLEITDMGVVGRNCTEDGWSEPFPHYFDACGFDDYEPESGDQDYYY  |       |       |       |       |       |       |
| *  | *     | **    | ***   | *     | *     | *     |
| TCWPTTPRGQAVVLDCLIFQLFAPIHGYNISRSCTEEGWSQLEPGPYHIACGLNDRASSLDEQQQTKFY  |       |       |       |       |       |       |
| 80   | 90    | 100   | 110   | 120   | 130   | 140   |
|  |       |       |       |       |       |       |
| 159  | 169   | 179   | 189   | 199   | 209   | 219   |
| LSVKALYTVGYSTSLATLTAMVILCRFRKLHCTRNIHMNLFVSFMLRAISVFIKDWILYAEQDSSHCF   |       |       |       |       |       |       |
| ****   | ***** | ***** | **    | **    | ***** | ***** |
| NTVKTGYTIGYSLASLLVAMAILSLFRKLHCTRNYIHMHLFMSFILRATAVFIKDMALFNSGEIDHCS   |       |       |       |       |       |       |
| 150  | 160   | 170   | 180   | 190   | 200   | 210   |
|  |       |       |       |       |       |       |
| 229  | 239   | 249   | 259   | 269   | 279   | 289   |
| VSTVECKAVMVFFHYCVVSNYFWLFIEGLYLFLLVETFFPERRYFYWYTIIGWGTPTVCVTWAVLRLY   |       |       |       |       |       |       |
| ***  | ***   | ***** | ***** | ***** | *     | ***** |
| EASVGCKAAVVFQYCVMANFFWLLVEGLYLYTLLAVSFFSERKYFWGYILIGWGVPSVFITIWTVVRIY  |       |       |       |       |       |       |
| 220  | 230   | 240   | 250   | 260   | 270   | 280   |
|  |       |       |       |       |       |       |
| 299  | 309   | 319   | 329   | 339   | 349   | 359   |
| FDDAGCWDMDSTALWWIKGPVVGSI MNFVLFIGIIILVQKLQSPDMGGNESSIYLRARSTLLIP      |       |       |       |       |       |       |
| ***  | ***   | ***** | ***** | **    | ***** | ***** |
| FEDFGCWDTIINSSLWWIIKAPILLSILVNFVLFICIIRILVQKLRPDPDIGKNDSSPYSRLAKSTLLIP |       |       |       |       |       |       |
| 290  | 300   | 310   | 320   | 330   | 340   | 350   |
|  |       |       |       |       |       |       |
| 369  | 379   | 389   | 399   | 409   | 419   | 429   |
| LFGIHYTVFAFSPENVSKRERLVFELGLGSFQGFVAVLYCFLNGEVQAEIKRKWRSWKVNRYFTMDFKH  |       |       |       |       |       |       |
| *****  | ****  | ***   | ***** | ***** | ***** | *     |
| LFGIHYVMFAFFPDNFKAQVKMFELVVGSGFQGFVAVLYCFLNGEVQAEILRRKWRRWHLQGVLGWSSKS |       |       |       |       |       |       |
| 360  | 370   | 380   | 390   | 400   | 410   | 420   |
|  |       |       |       |       |       |       |
| 439  | 449   | 459   |       |       |       |       |
| RHPSLASSGVNGGTQLSILSKSSSQLRMSSLPADNLAT*                                |       |       |       |       |       |       |
| **   | **    | *     | ***** | **    | *     | ***   |
| QHPWGSNGATCSTQVSMLTRVSPSARRSSSFQAEVSLV                                 |       |       |       |       |       |       |
| 430  | 440   | 450   |       |       |       |       |

FIG.20

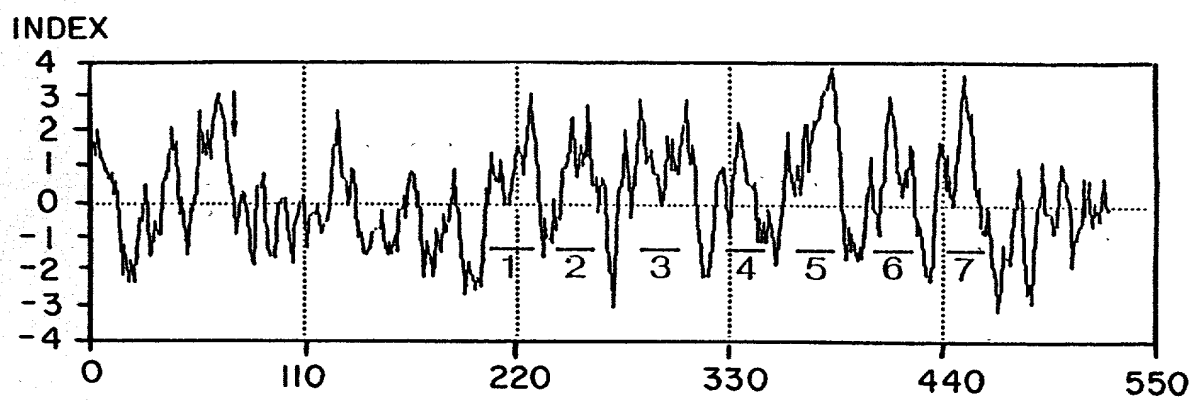


FIG. 21

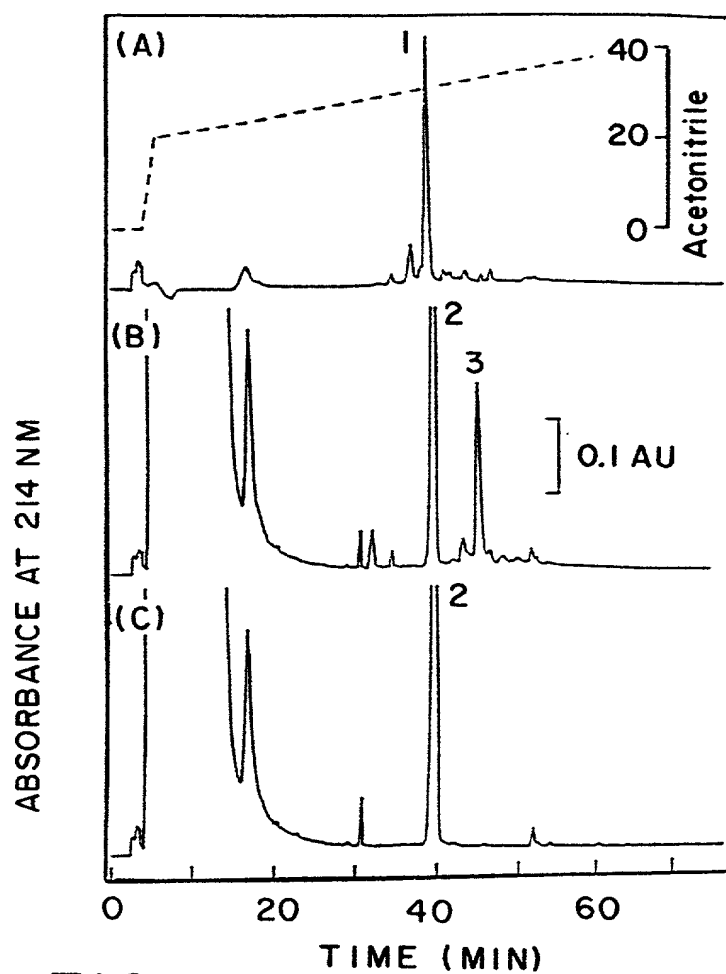


FIG. 28

small gaps only when gaps are at the ends of the sequence  
 gaps are only at the ends of the sequence

10 20 30 40 50 60 70 80  
 MAGVHVSLA AHCACPWGR GRLRKGRAC KSAAQRHIGA DPLLSVGGQ WQPRSVMAQ WLVSLAALL LLPMAFAMHS  
 .....  
 ..... MRGGRIHPEP PQRRLSVMAS IAOVSLAALL LLPMAFAMHS  
 .....  
 .....  
 ..... MAR LQSLAALL LLPMAFAMHS

HUMAN  
 BOVINE  
 RAT

90 100 110 120 130 140 150 160  
 DCIFKKEQAM CLEKIQORANE LMGENDSSPG CPGMNDNITC WKPAHVGEV LVSCPELFRI FNPQVWETE TIGESDFGDS  
 DCIFKKEQAM CLEKIQORVND LMGLNDSSPG CPGMNDNITC WKPAHVGEV LVSCPELFRI FNPQVWETE TIGEFGFADS  
 DCIFKKEQAM CLEKIQORAND LMGLNESSPG CPGMNDNITC WKPAHVGEV LVSCPELFRI FNPQVWETE TIGDSGFADS

170 180 190 200 210 220 230 240  
 NSLDLSDMGV VSRNCTEDGW SEFPFHYFDA CGFDEYESET GDQVYYLSV KALYTVGYST SLVTLTTAMV ILCRFRKLHC  
 KSLDLSOMV VSRNCTEDGW SEFPFHYFDA CGFDEYESET GDQVYYLSV KALYTVGYST SLVTLTTAMV ILCRFRKLHC  
 NSLEITDMGV VSRNCTEDGW SEFPFHYFDA CGFDEYESET GDQVYYLSV KALYTVGYST SLVTLTTAMV ILCRFRKLHC

250 260 270 280 290 300 310 320  
 TRNFIHMNLF VSFMLRAISV FIKDWILYAE QDSNHCFVST VECKAVMVFF HYCVWSNYFW LFIEGLYFLT LLVETFFPER  
 TRNFIHMNLF VSFMLRAISV FIKDWILYAE QDSNHCFVST VECKAVMVFF HYCVWSNYFW LFIEGLYFLT LLVETFFPER  
 TRNFIHMNLF VSFMLRAISV FIKDWILYAE QDSNHCFVST VECKAVMVFF HYCVWSNYFW LFIEGLYFLT LLVETFFPER

330 340 350 360 370 380 390 400  
 RYFYWYTIIG WGTPTVCVTV WAILRLYFDD TGCWDMNDST ALWVWIKGPV VGSIMWNVFL FIGIIVILVQ KLOSPDMGGN  
 RYFYWYTIIG WGTPTVCVTV WAILRLYFDD TGCWDMNDST ALWVWIKGPV VGSIMWNVFL FIGIIVILVQ KLOSPDMGGN  
 RYFYWYTIIG WGTPTVCVTV WAILRLYFDD TGCWDMNDST ALWVWIKGPV VGSIMWNVFL FIGIIVILVQ KLOSPDMGGN

410 420 430 440 450 460 470 480  
 ESSIV-----  
 ESSIVFSCVQ KCYCKPQRAQ QHSCDMSELS TITLRLARST LLLIPLFGIH YTVFAFSPEN VSKRERLVFE LGLGSFQGFV  
 ESSIVFSCVQ KCYCKPQRAQ QHSCDMSELS TITLRLARST LLLIPLFGIH YTVFAFSPEN VSKRERLVFE LGLGSFQGFV

490 500 510 520 530 540 550  
 VAVLYCFLNG EVOAEIKRKW RSWKVNRYFA VDFKHRHPSL ASSGVNGGTQ LSILSKSSQ IRMSGLPADN LAT  
 VAVLYCFLNG EVOAEIKRKW RSWKVNRYFT MDFKHRHPSL ASSGVNGGTQ LSILSKSSQ IRMSGLPADN LAT  
 VAVLYCFLNG EVOAEIKRKW RSWKVNRYFT MDFKHRHPSL ASSGVNGGTQ LSILSKSSQ IRMSGLPADN LAT

FIG. 22



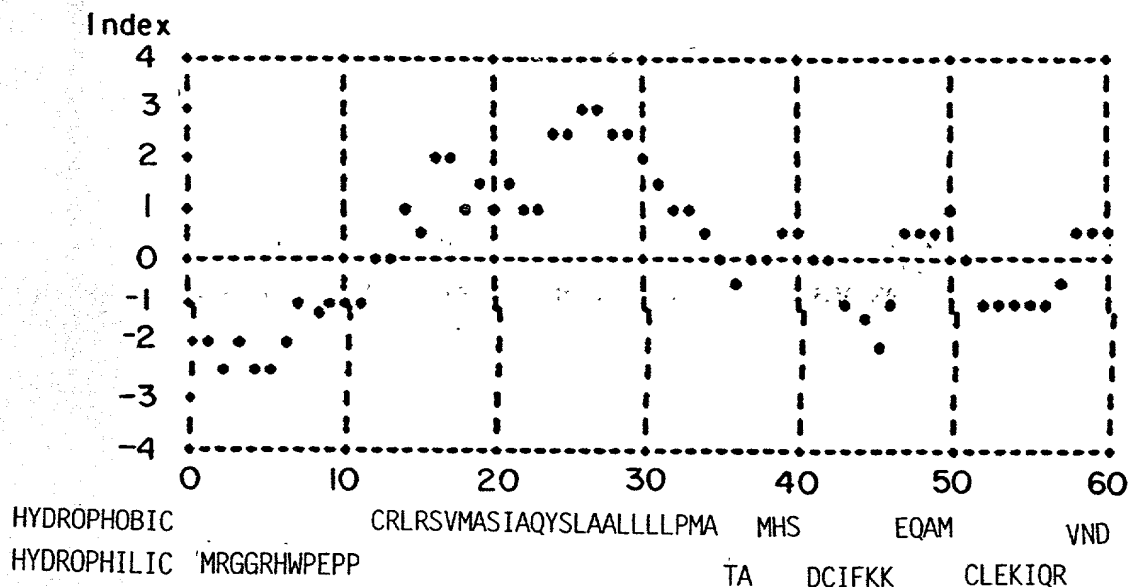


FIG.23A

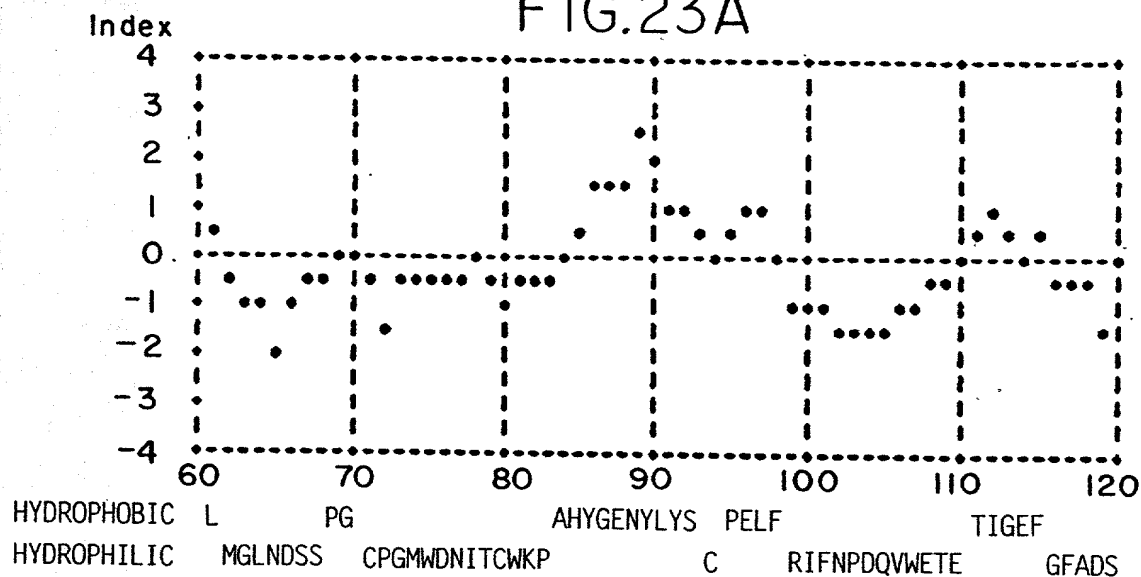


FIG.23B

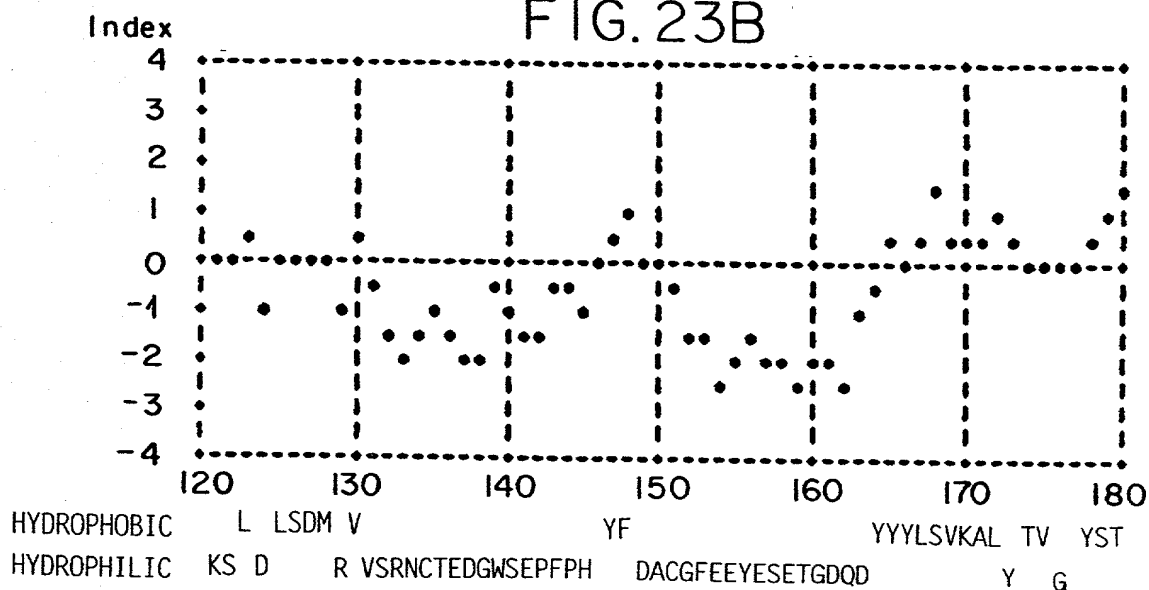


FIG.23C

COPY OF  
ORIGINAL

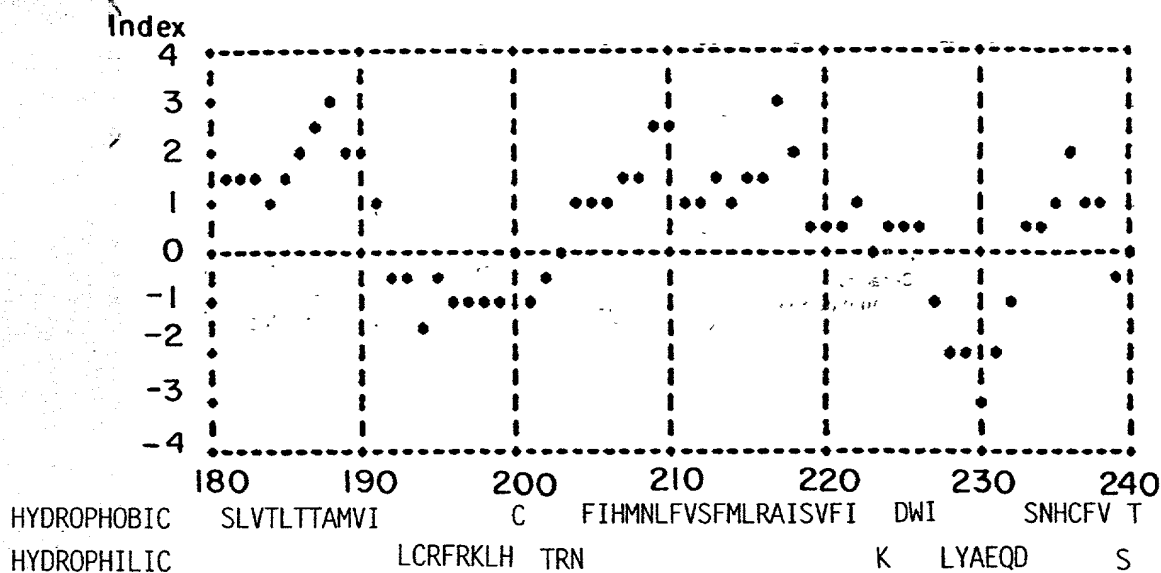


FIG.23D

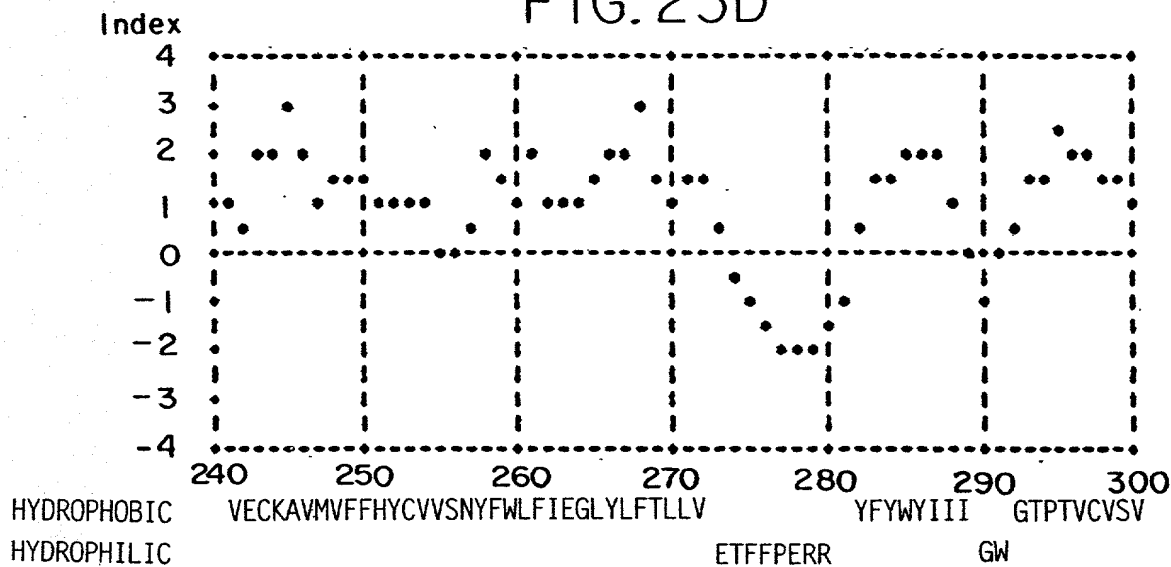


FIG.23E

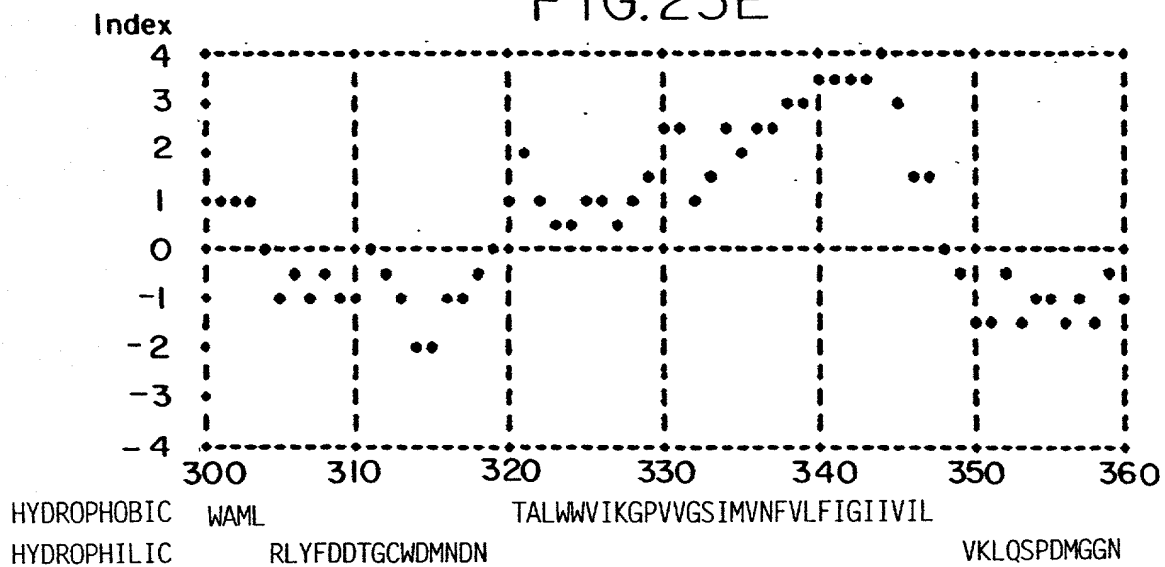


FIG.23F

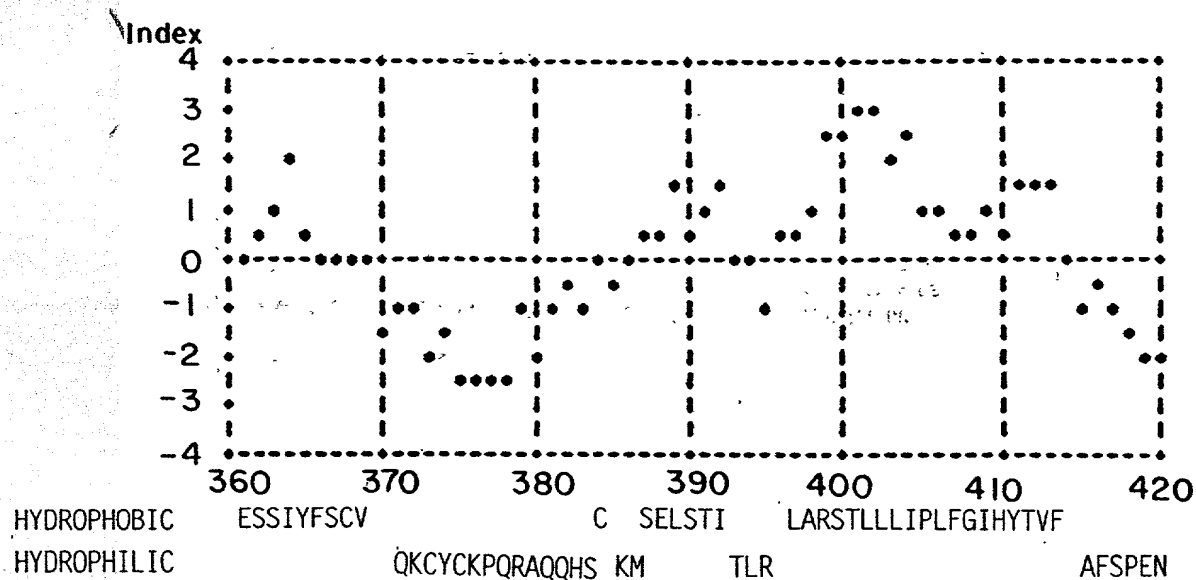


FIG. 23G

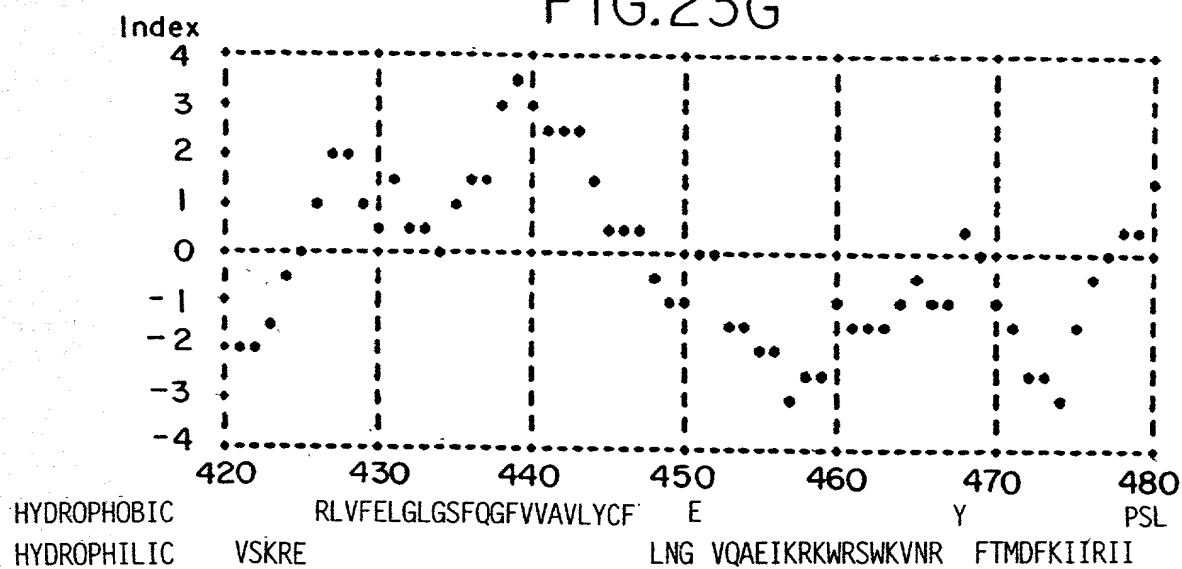


FIG. 23H

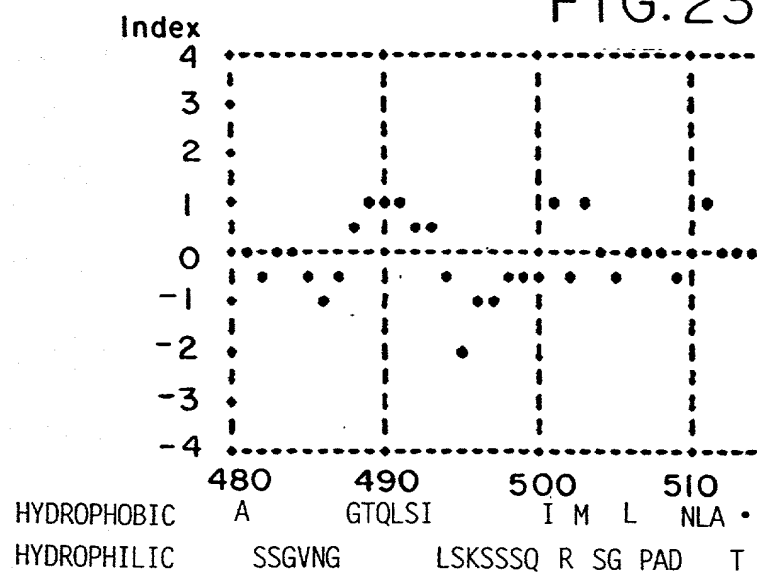


FIG. 23I

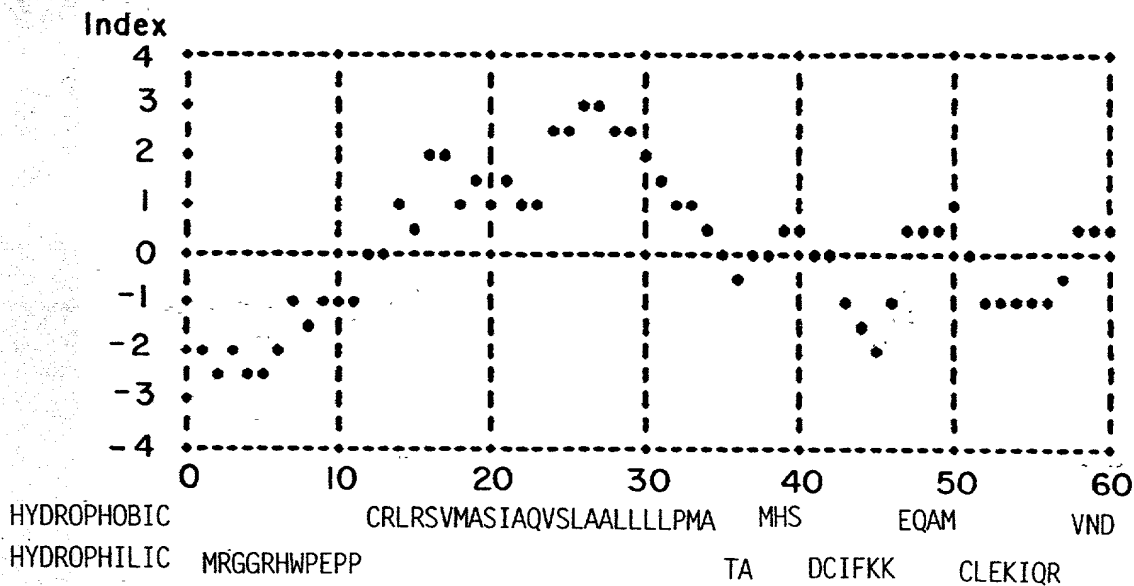


FIG.24A

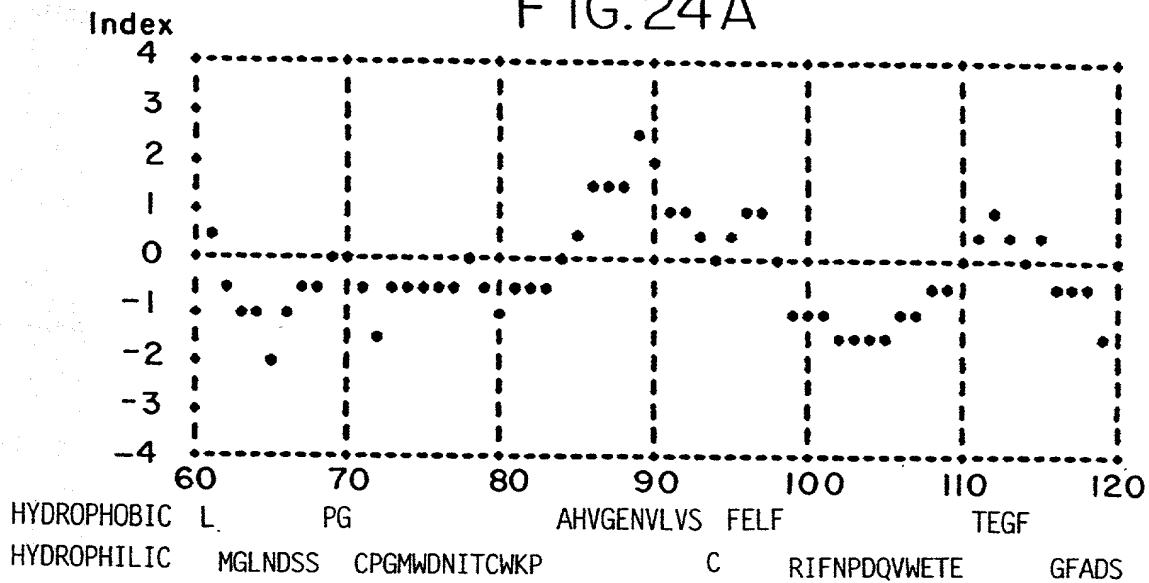


FIG.24B

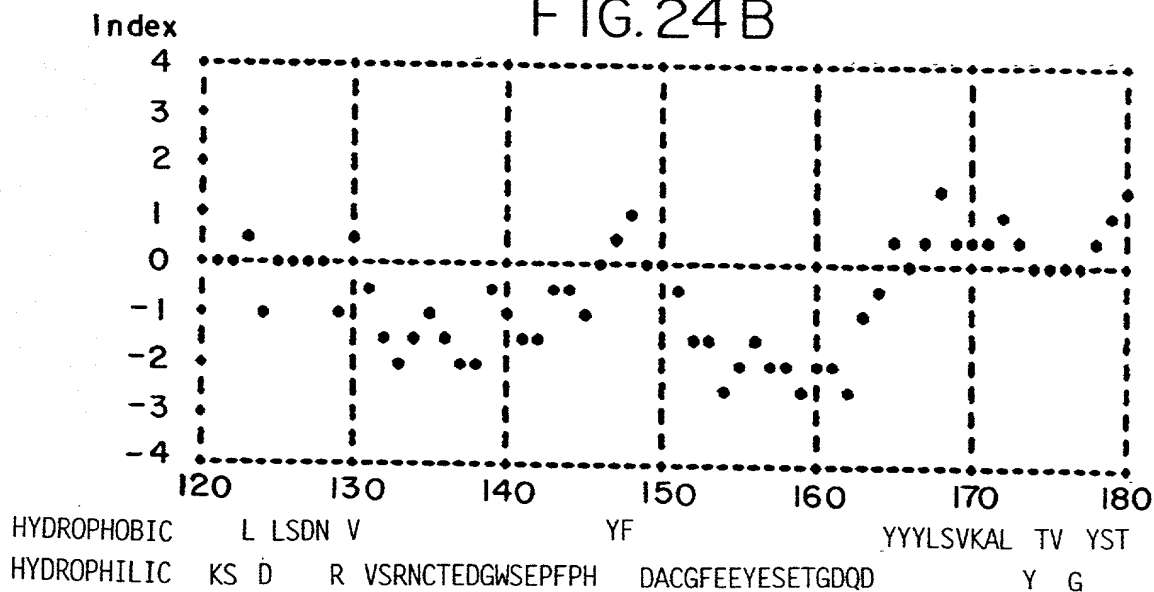


FIG.24C

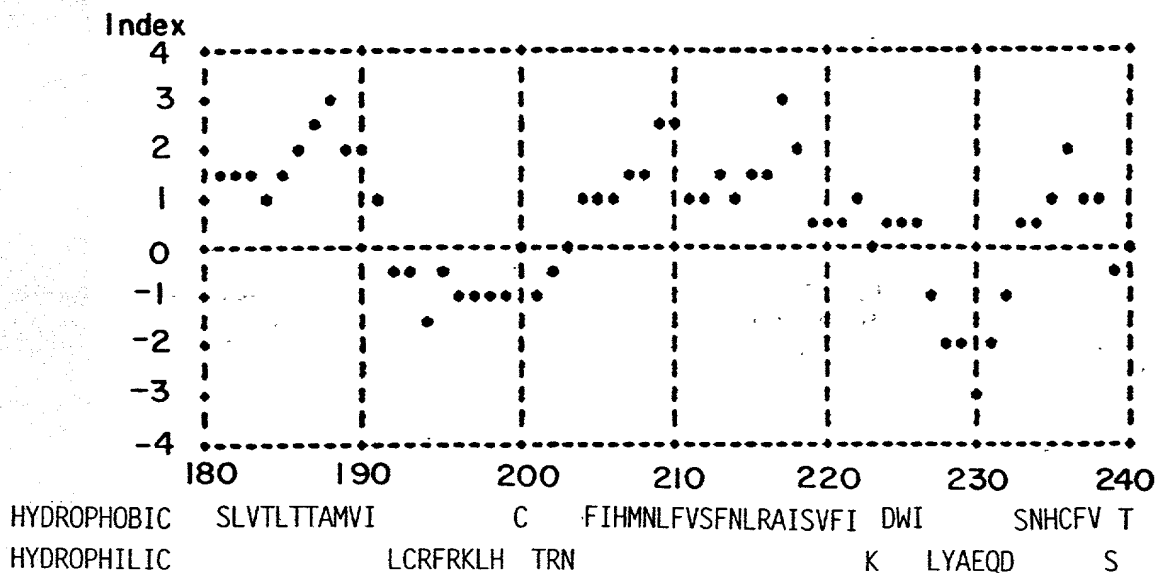


FIG. 24D

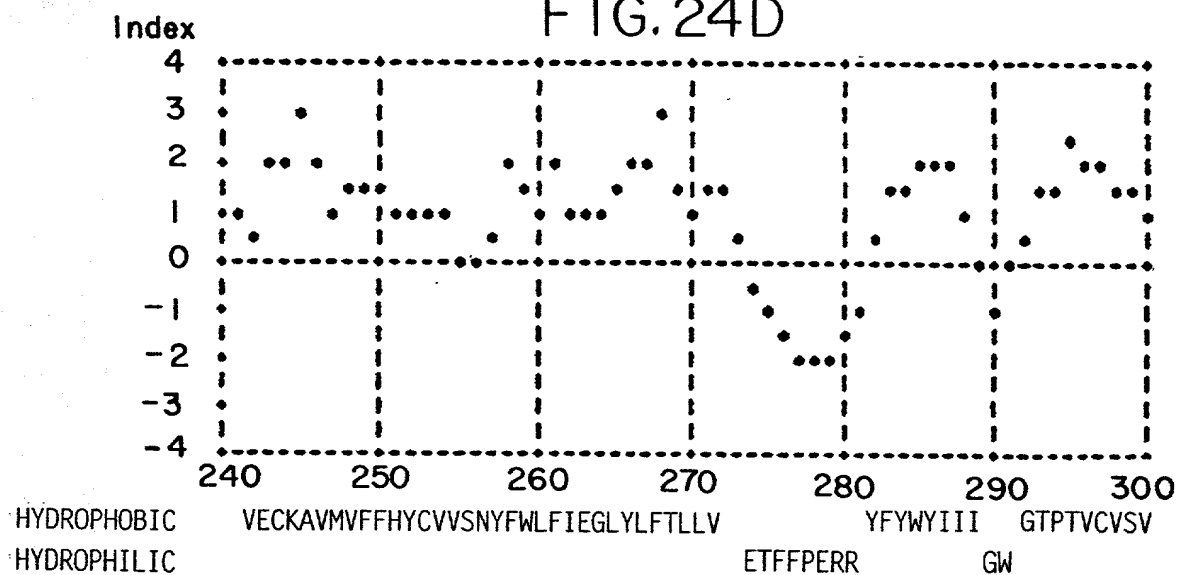


FIG. 24E

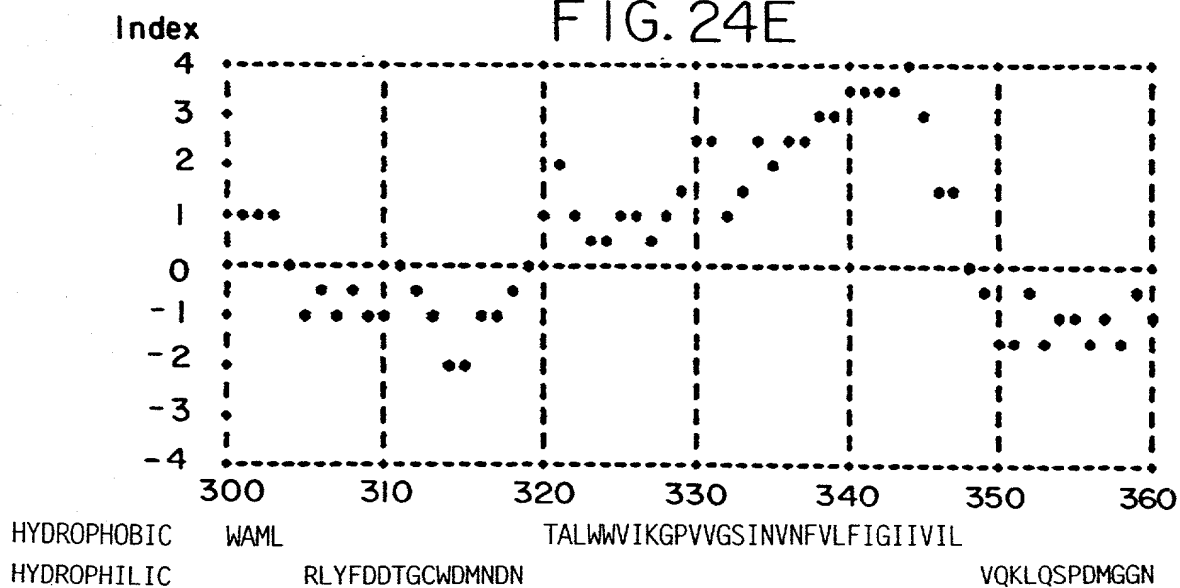


FIG. 24F

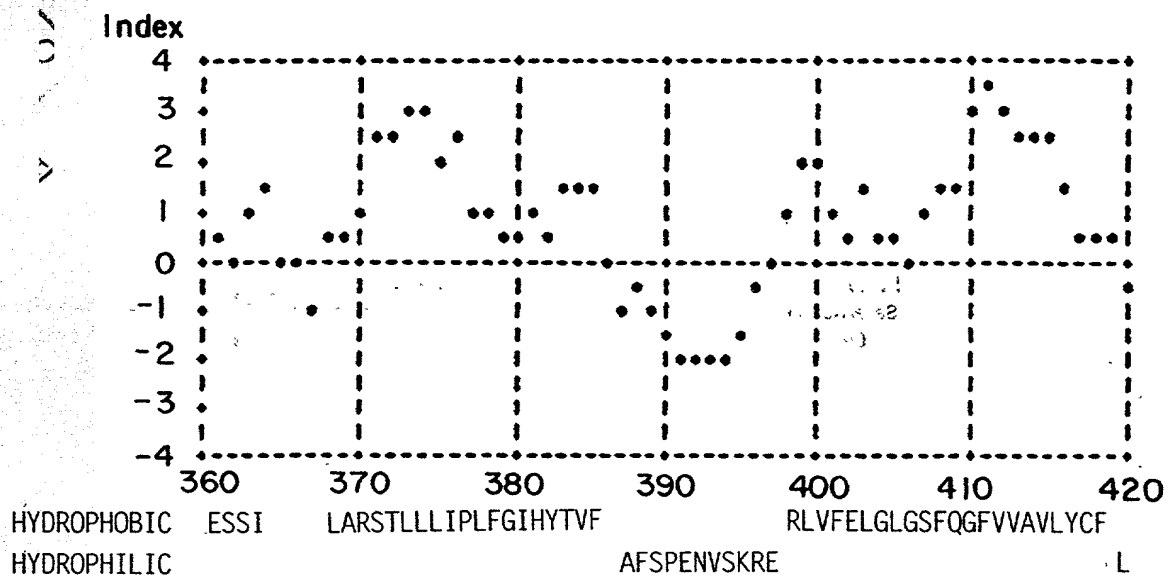


FIG. 24G

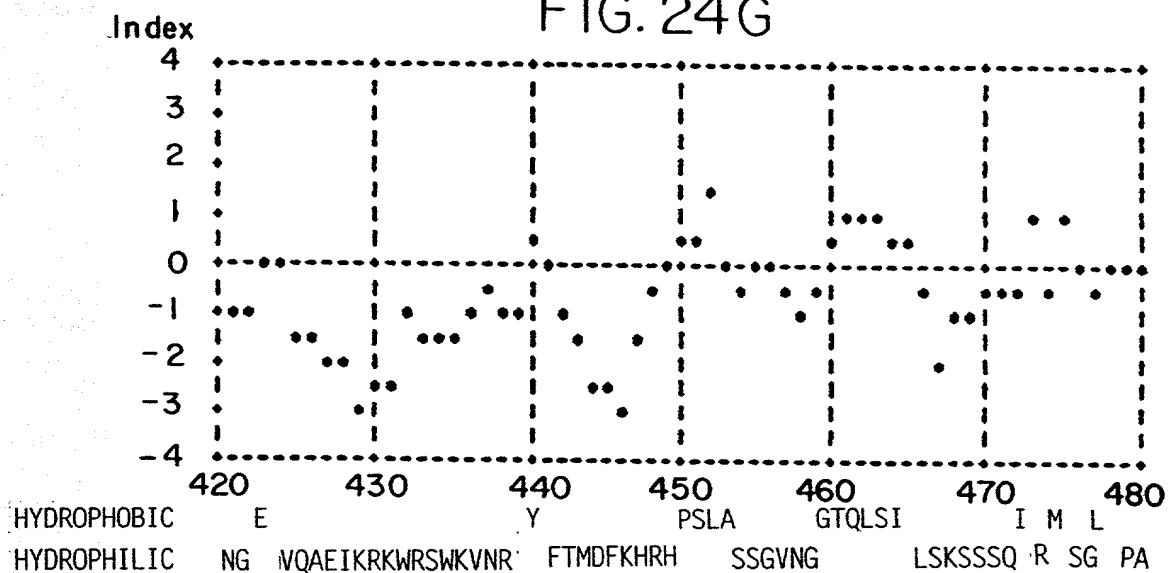


FIG. 24H

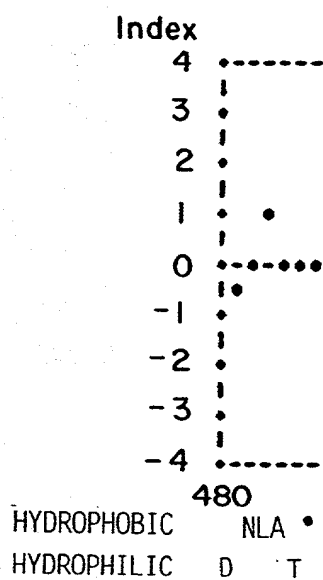


FIG. 24I

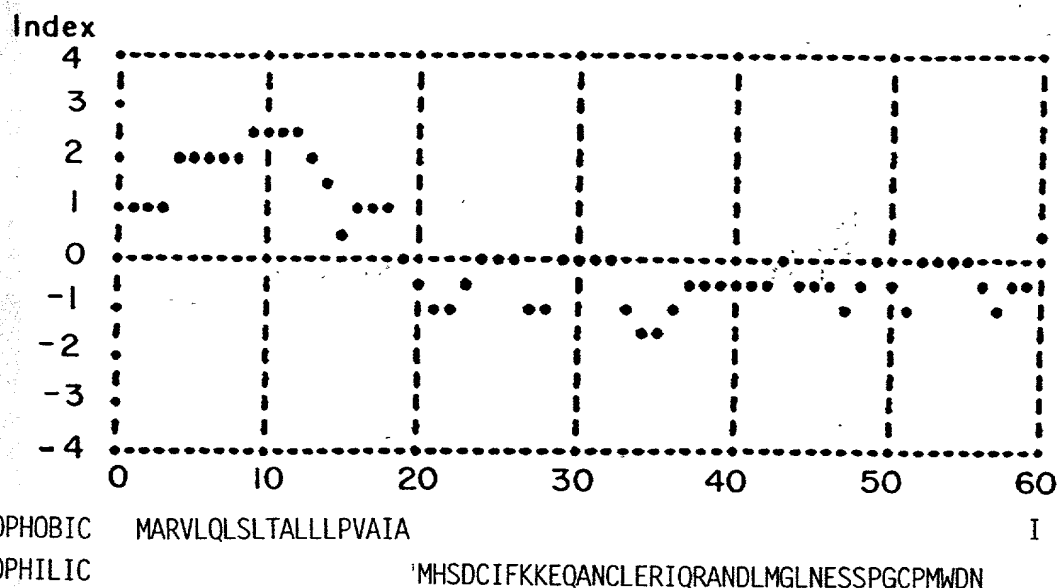


FIG.25A

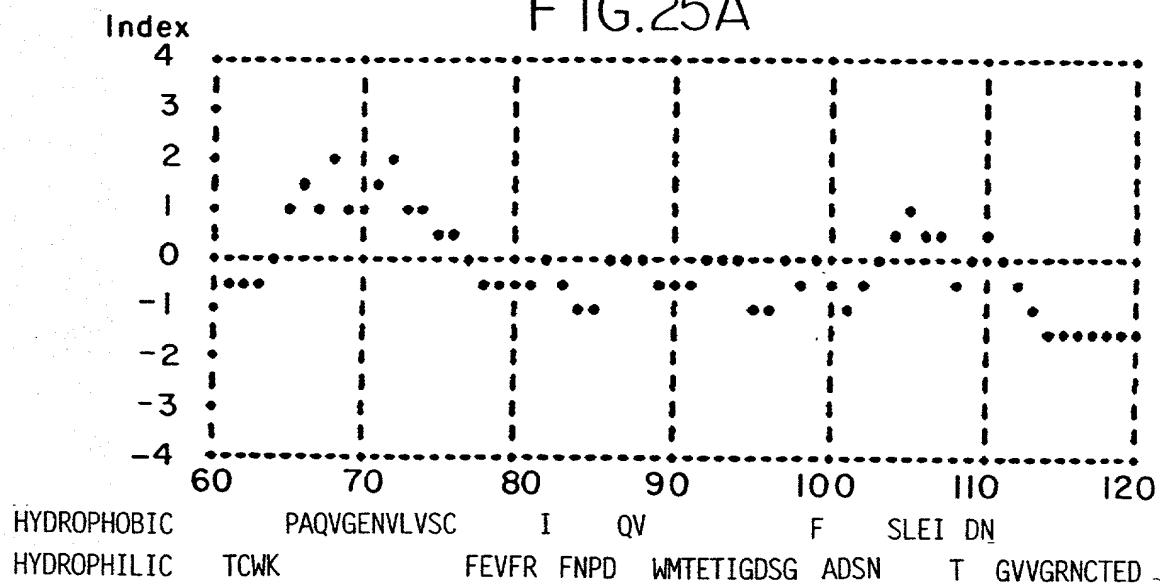


FIG.25B

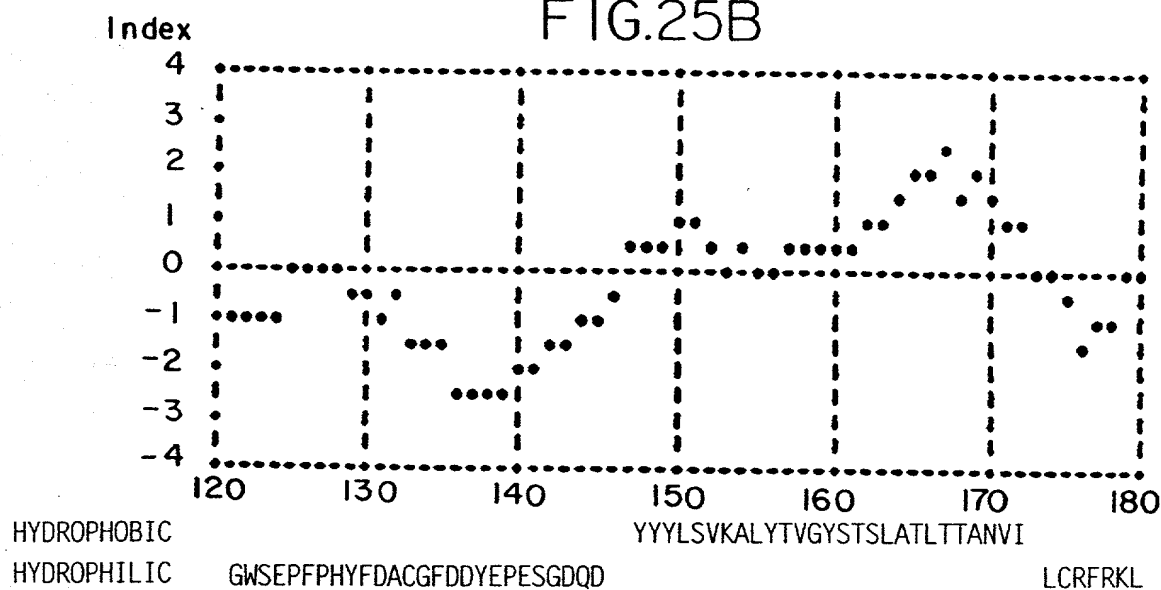


FIG.25C

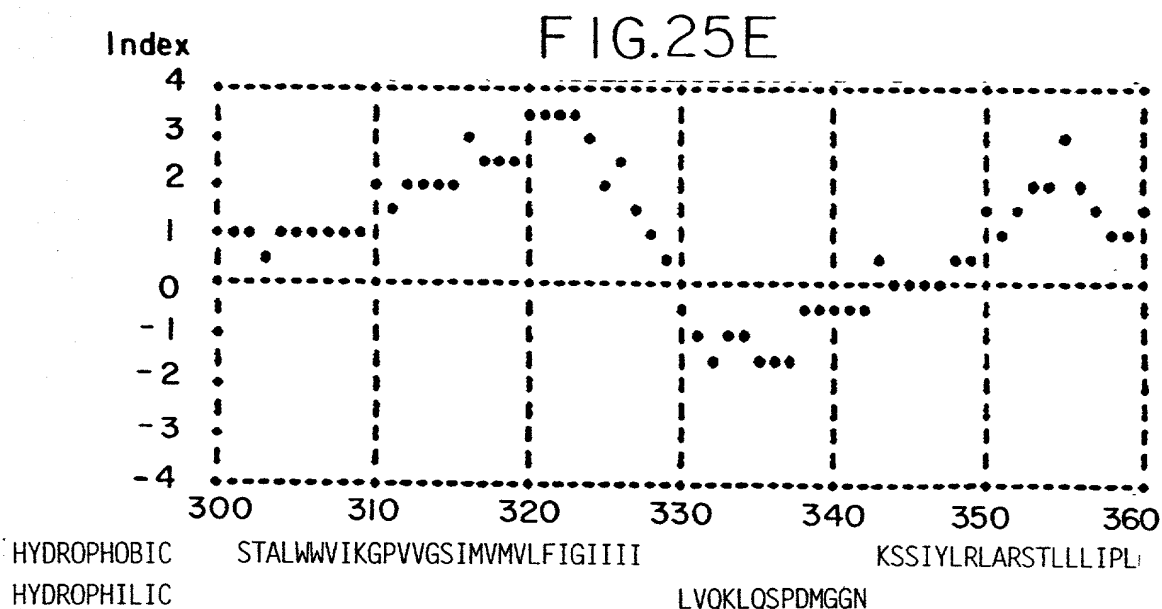
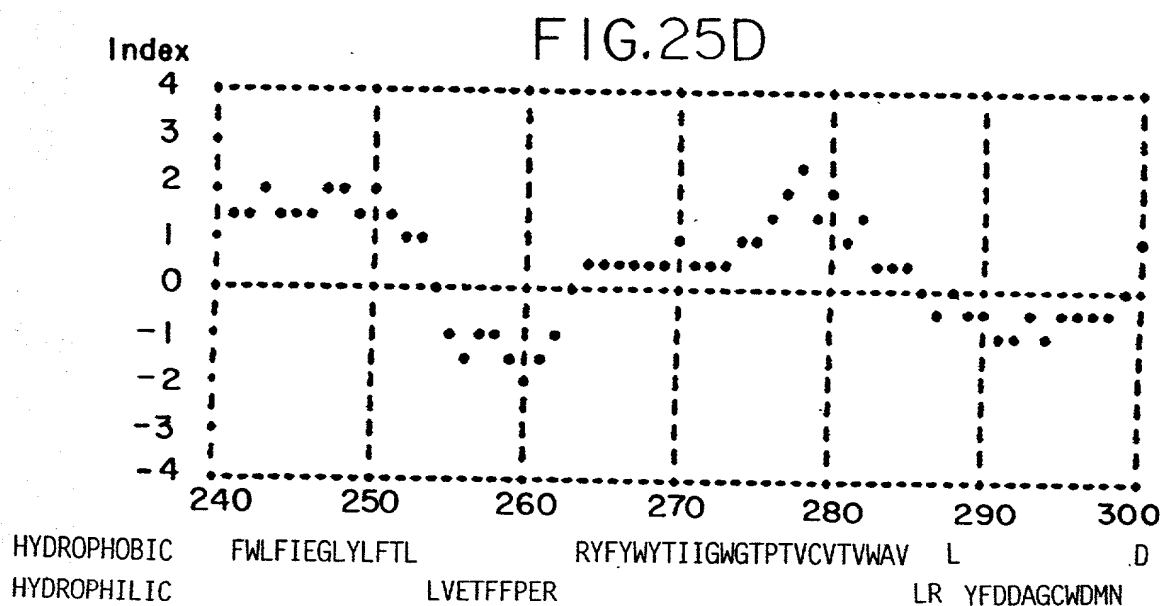
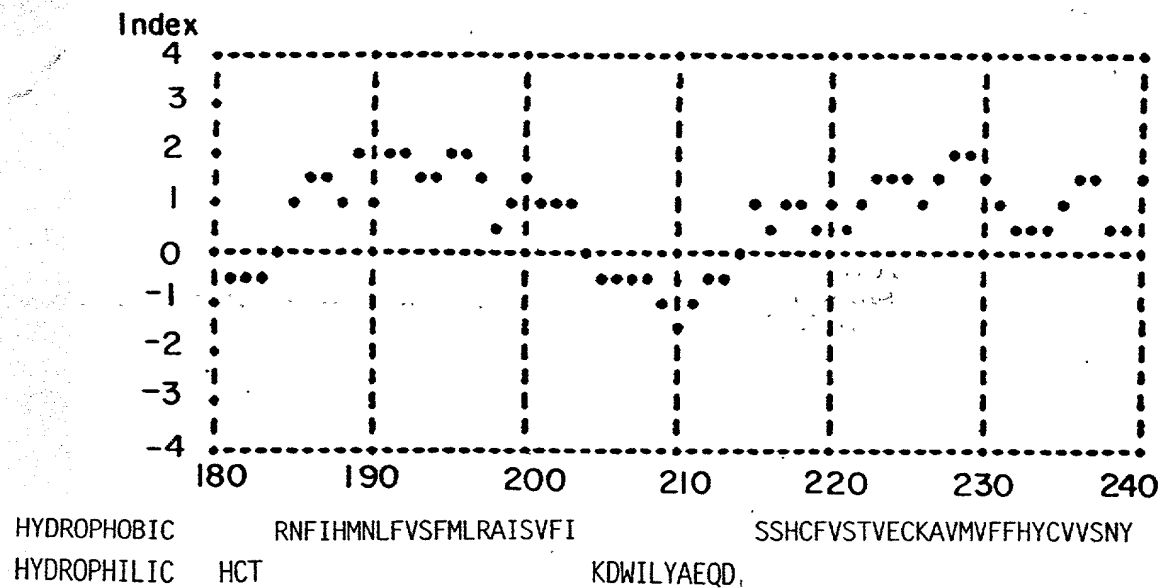
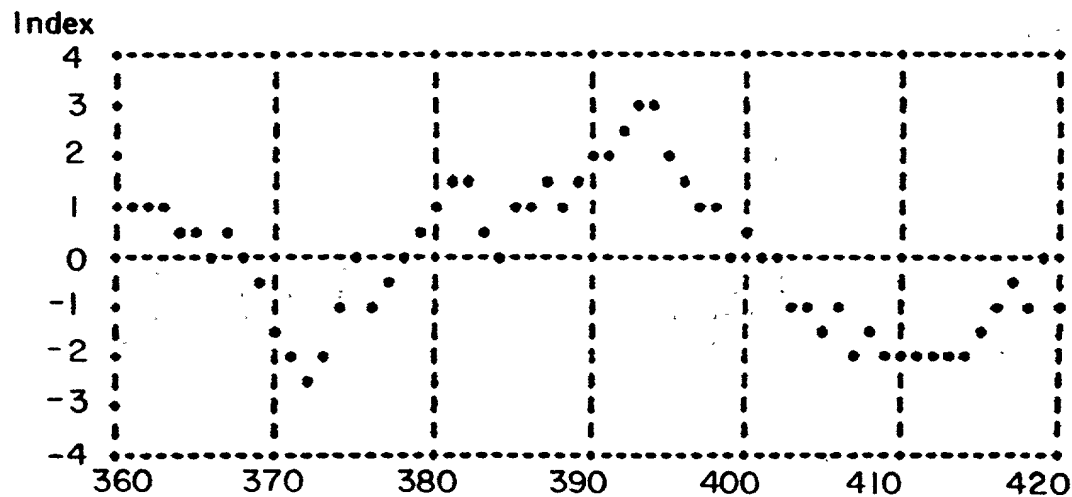


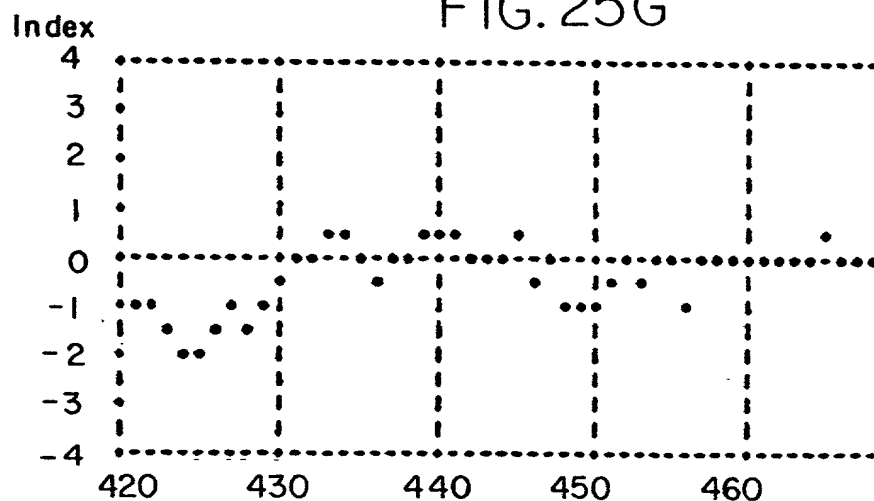
FIG.25F





HYDROPHOBIC FGIHTYVF ERLVEFELGLGSFQGFVVAVLYC  
 HYDROPHILIC AFSPENVSKR FLNGEVQAEIKKKWRSWKVN

FIG. 25G



HYDROPHOBIC HPSL VNGGTQL I QL MSSL NLA •  
 HYDROPHILIC RYFTMDFKHR ASSG S LSKSSS R PAD T

FIG. 25H

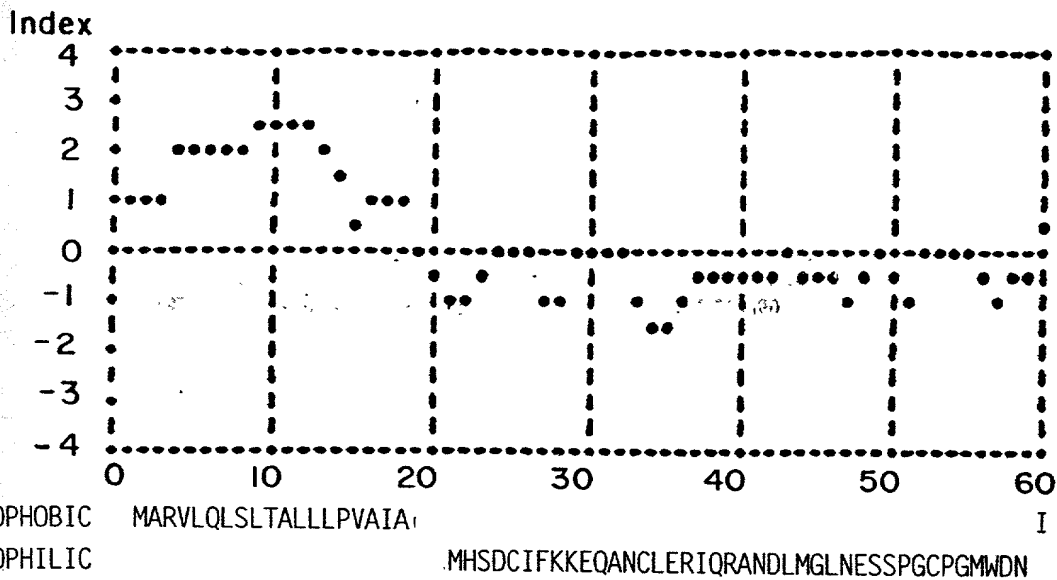


FIG.26A

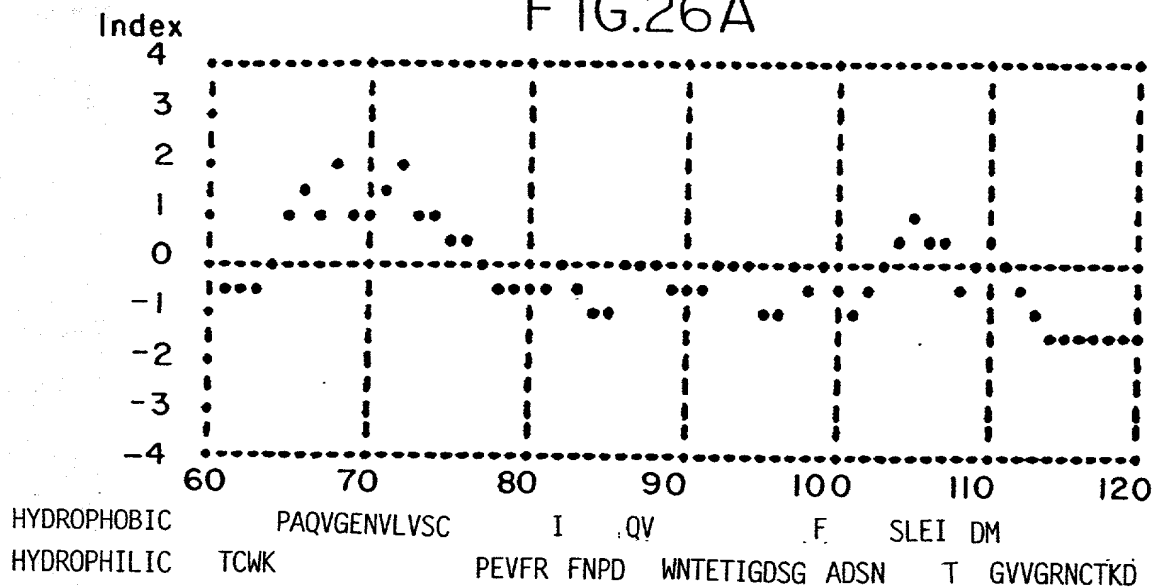


FIG.26B

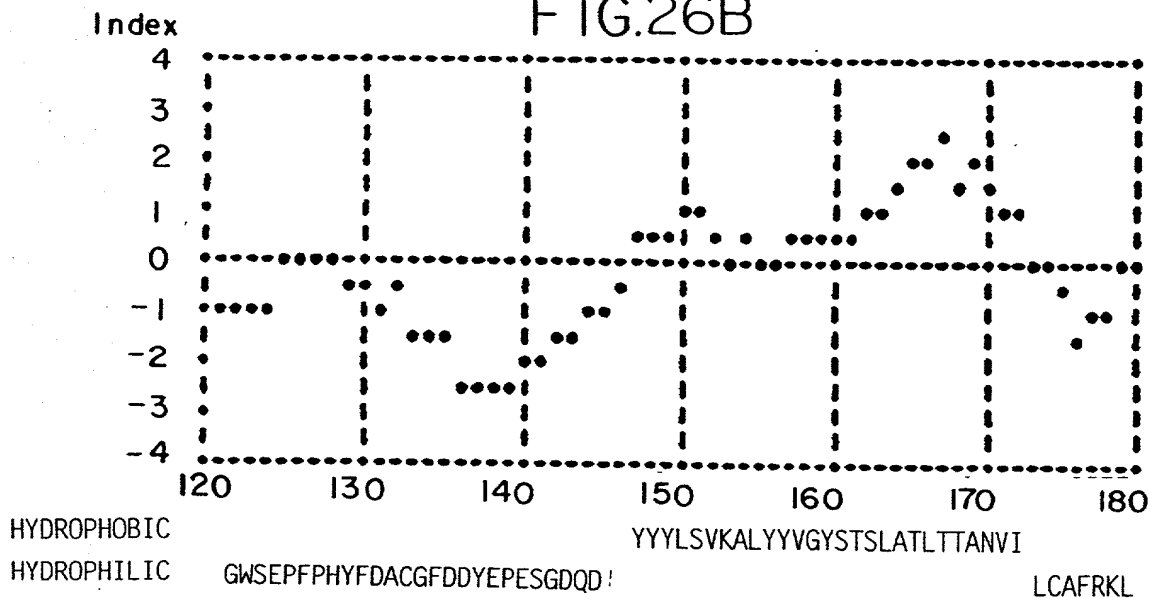


FIG.26C

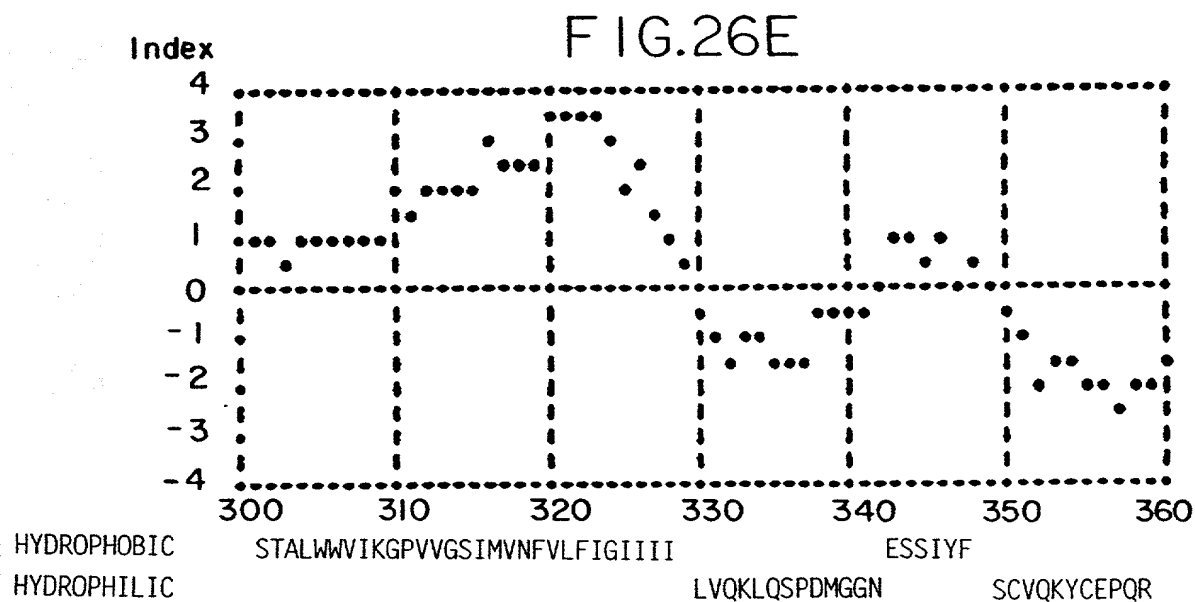
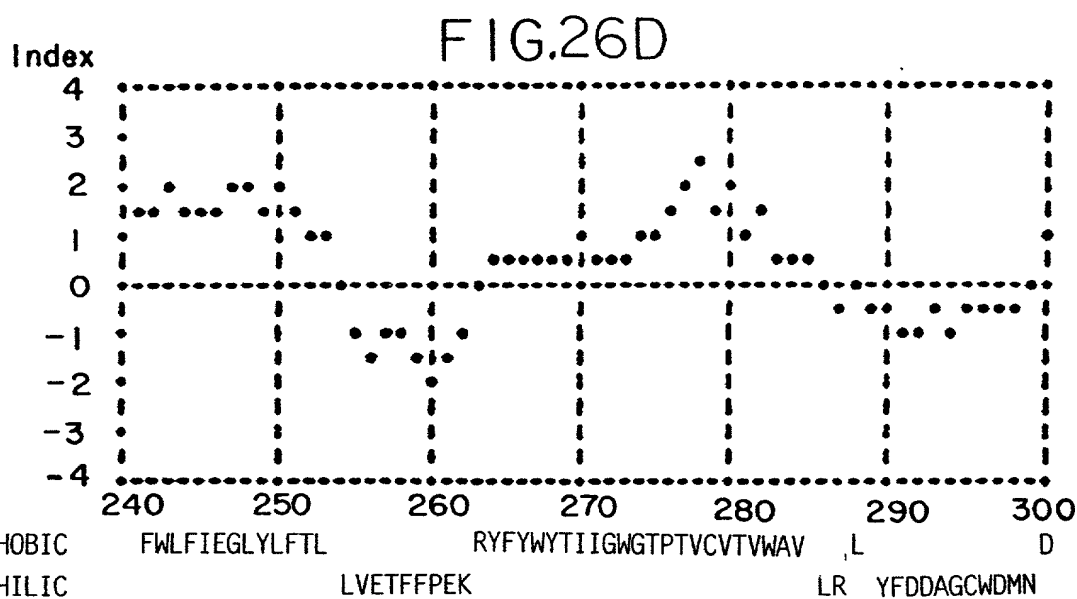
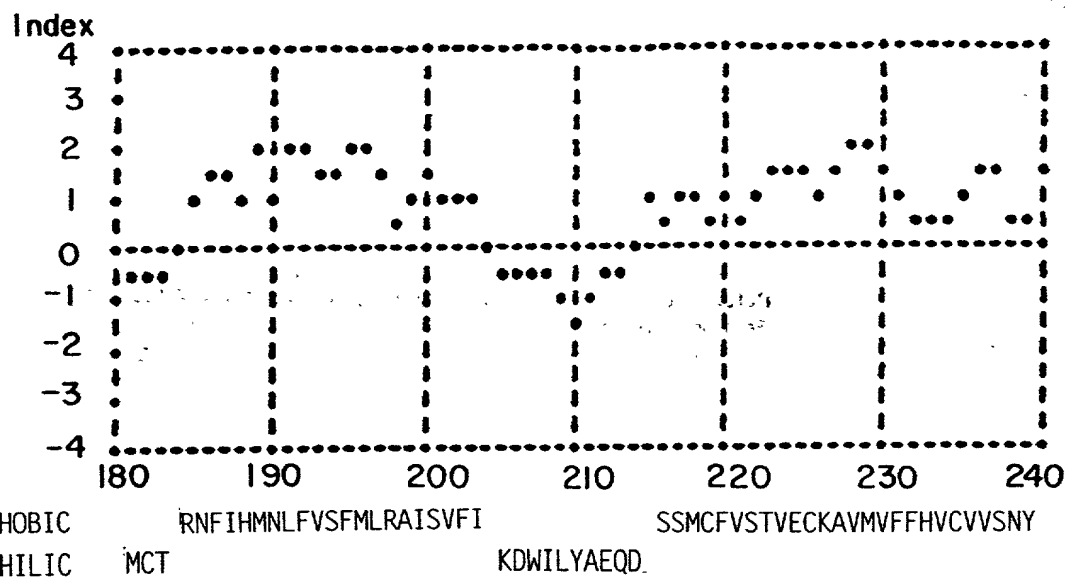
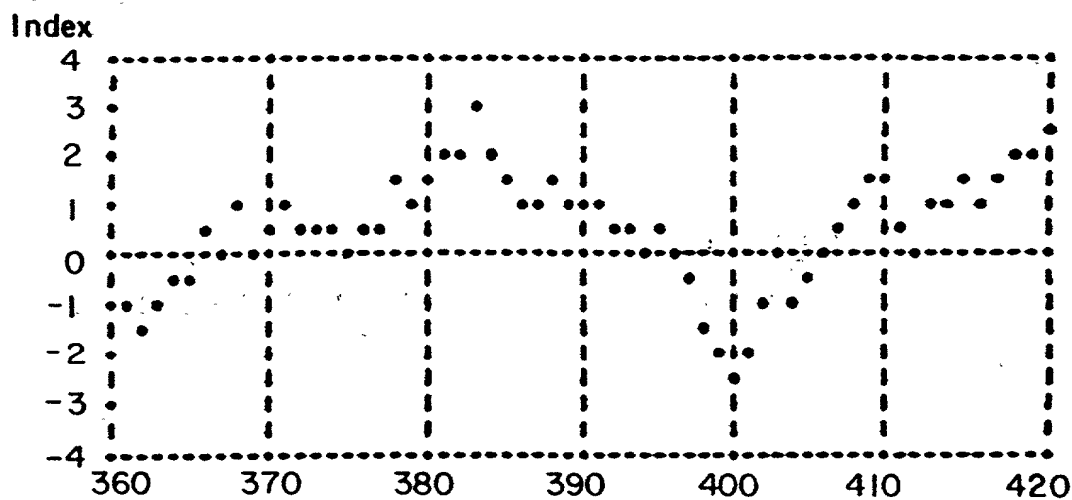
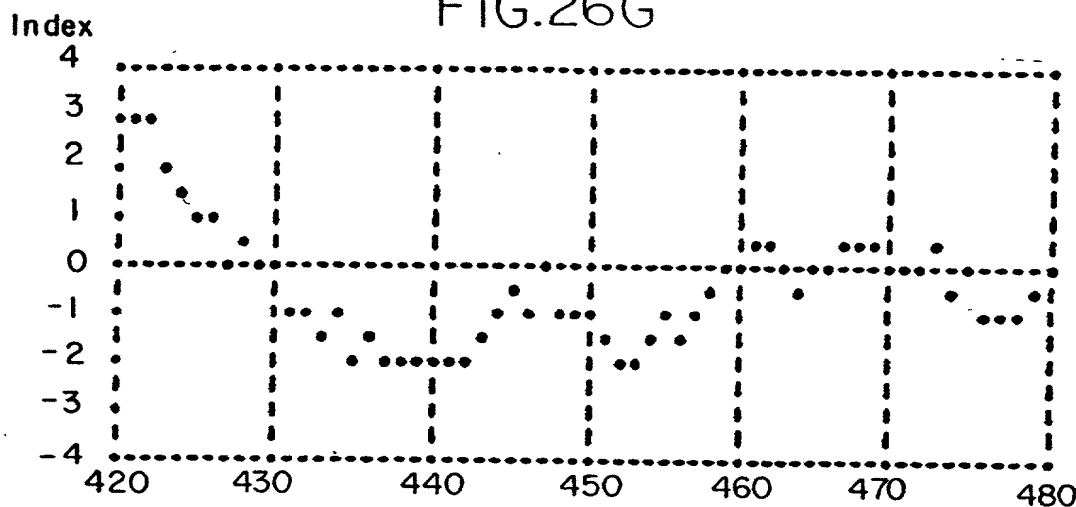


FIG. 26F



HYDROPHOBIC C MSELSTITRLARSTILLIPLFGIMYTVF ERLVFELGLGSFQG  
 HYDROPHILIC AQHS K. AFSPENVSKR

FIG.26G



HYDROPHOBIC FWVAVLYC MPSL VMGGTQL I  
 HYDROPHILIC FLNGEVQAEIKRKWRSWKVNRFTNDFEMR ASSG S LSRSS

FIG.26H

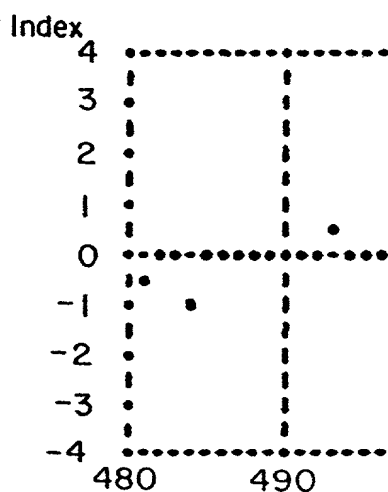


FIG.26I

HYDROPHOBIC QL MSSL NLA •  
 HYDROPHILIC S R PAD T

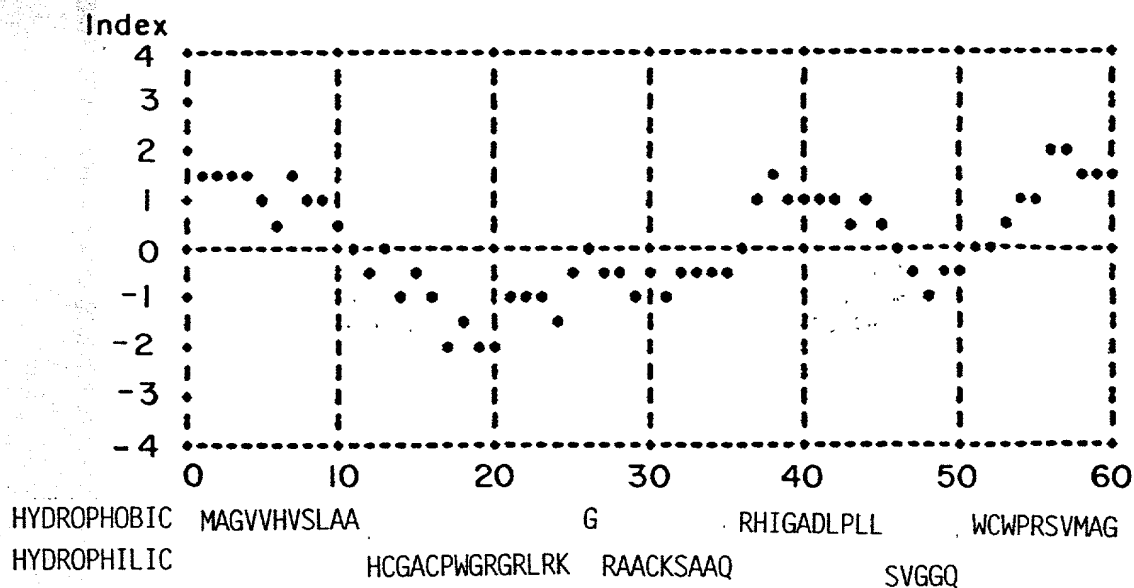


FIG.27A

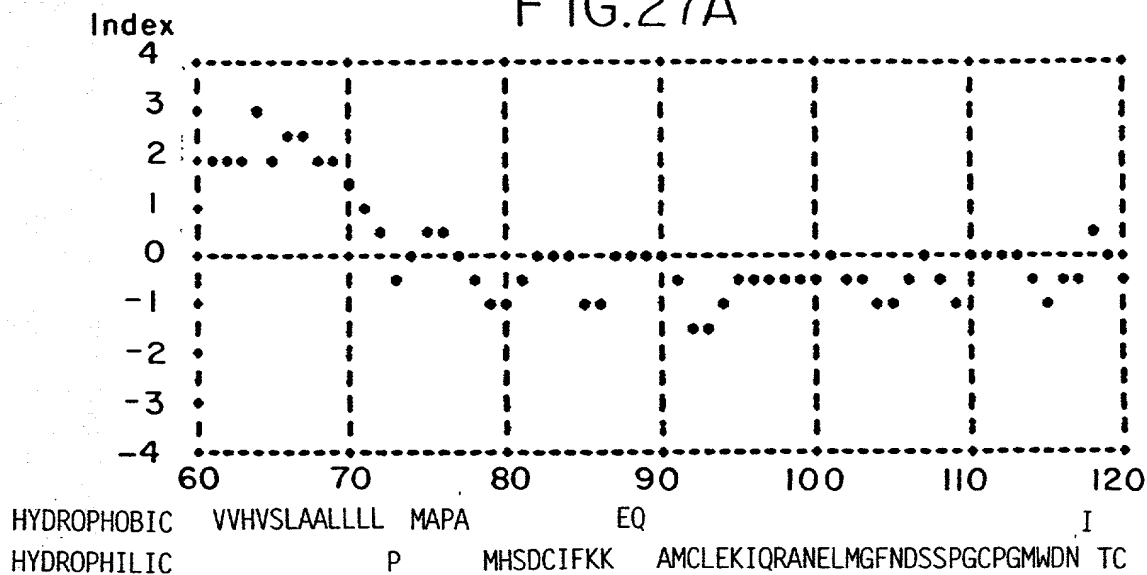


FIG.27B

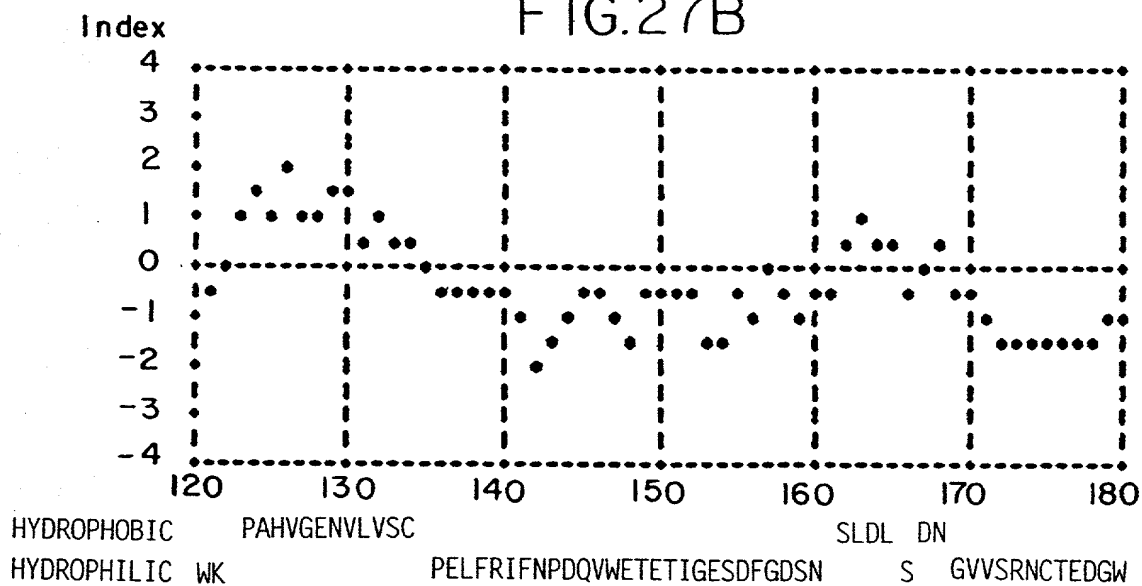


FIG.27C

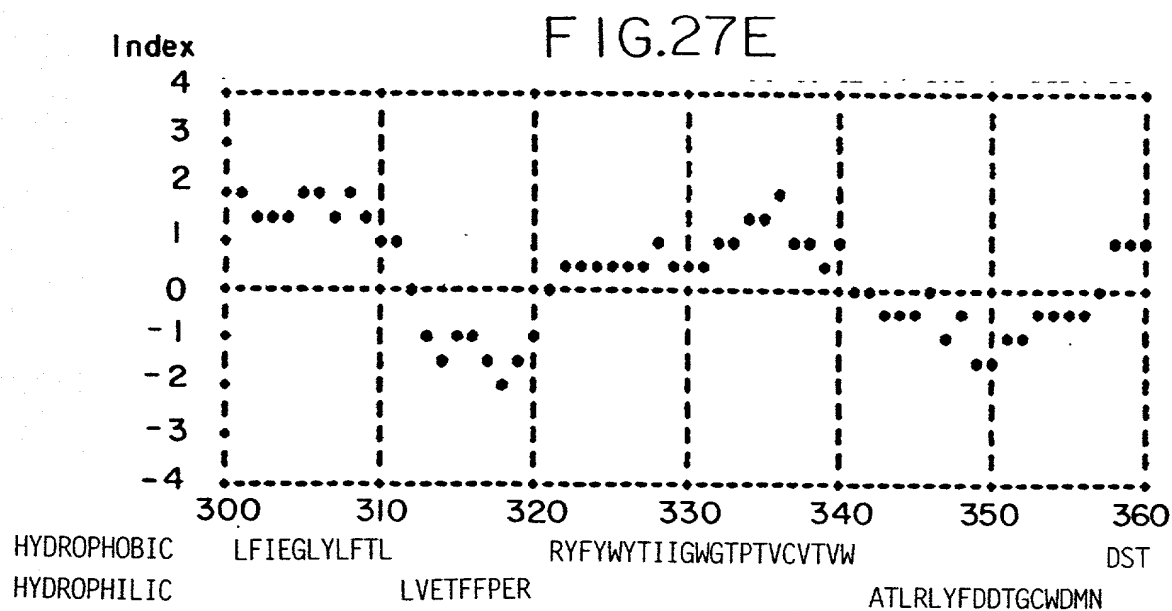
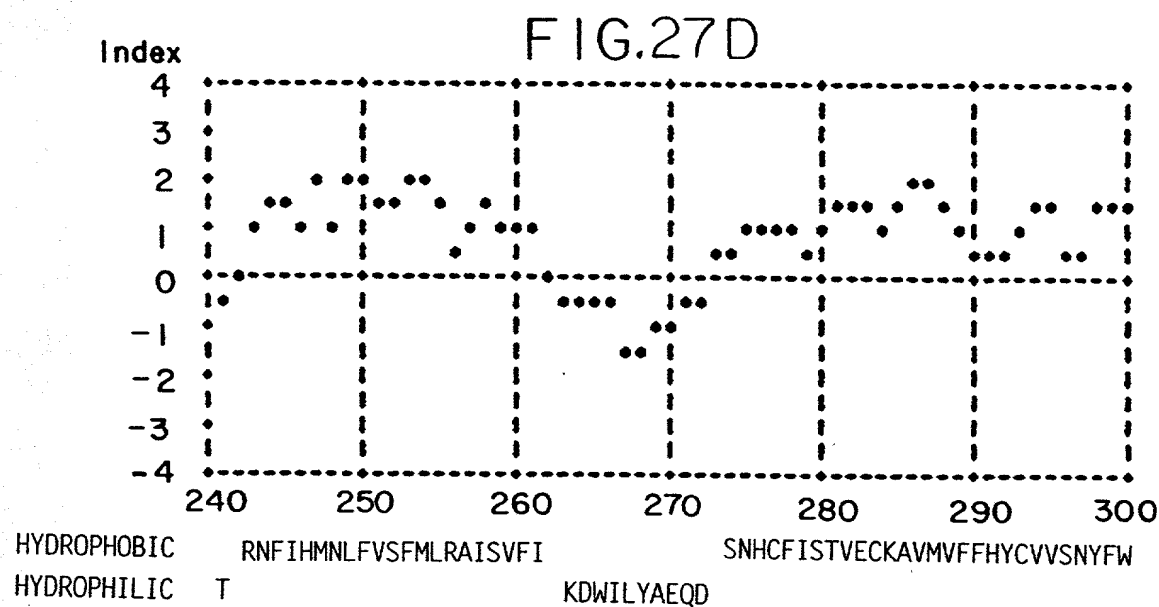
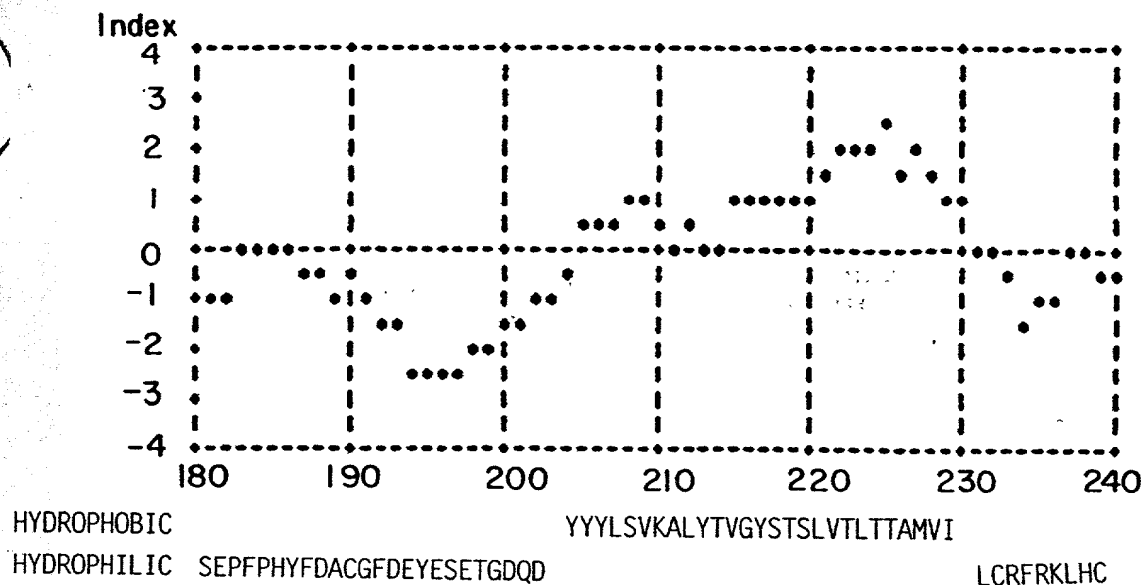


FIG.27F

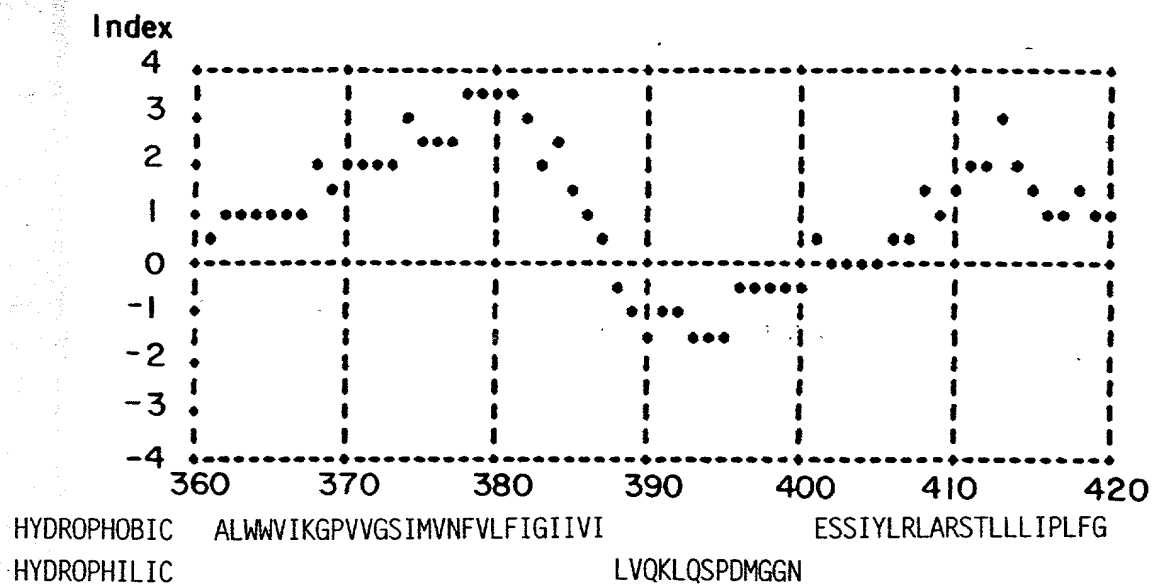


FIG. 27G

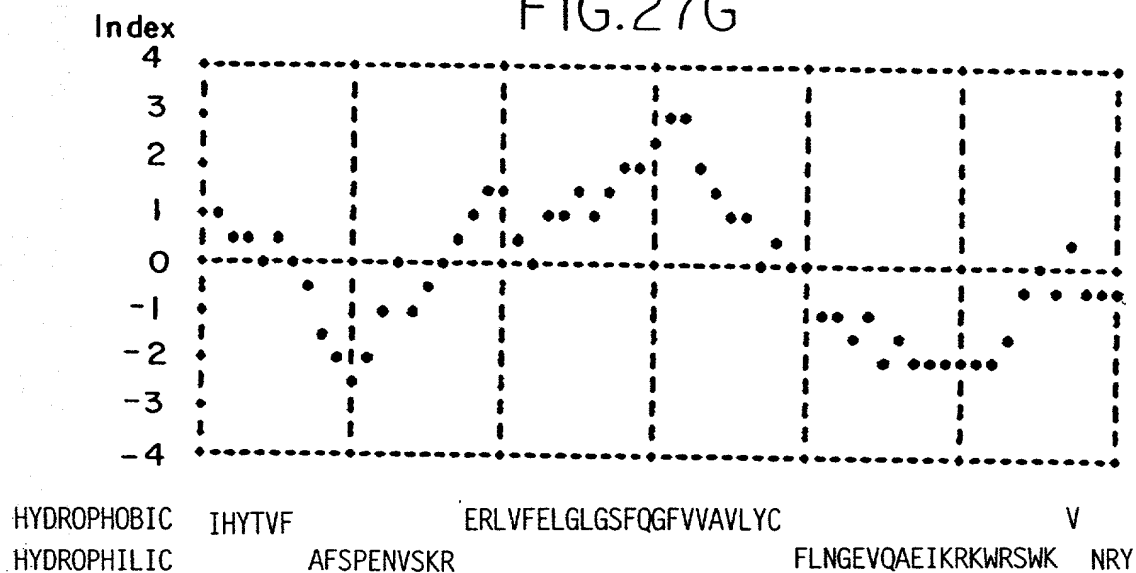
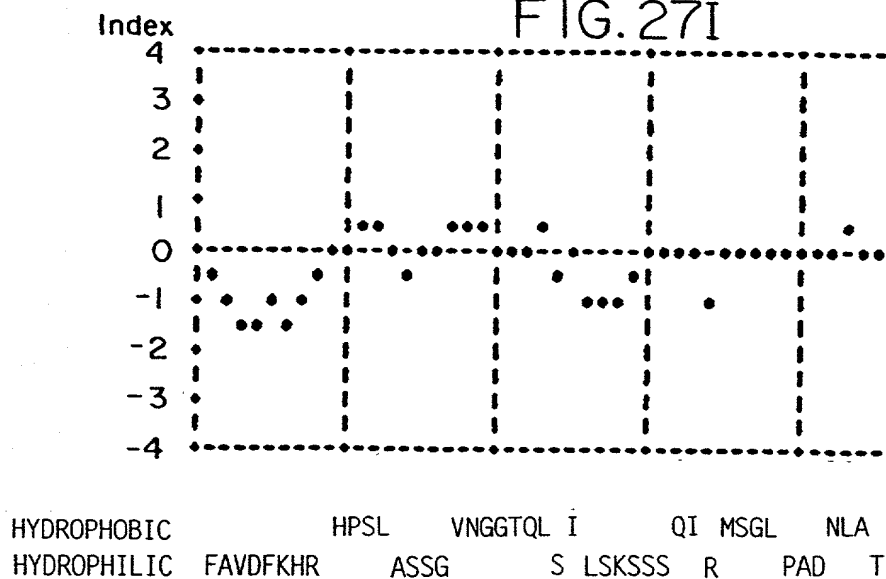


FIG. 27I



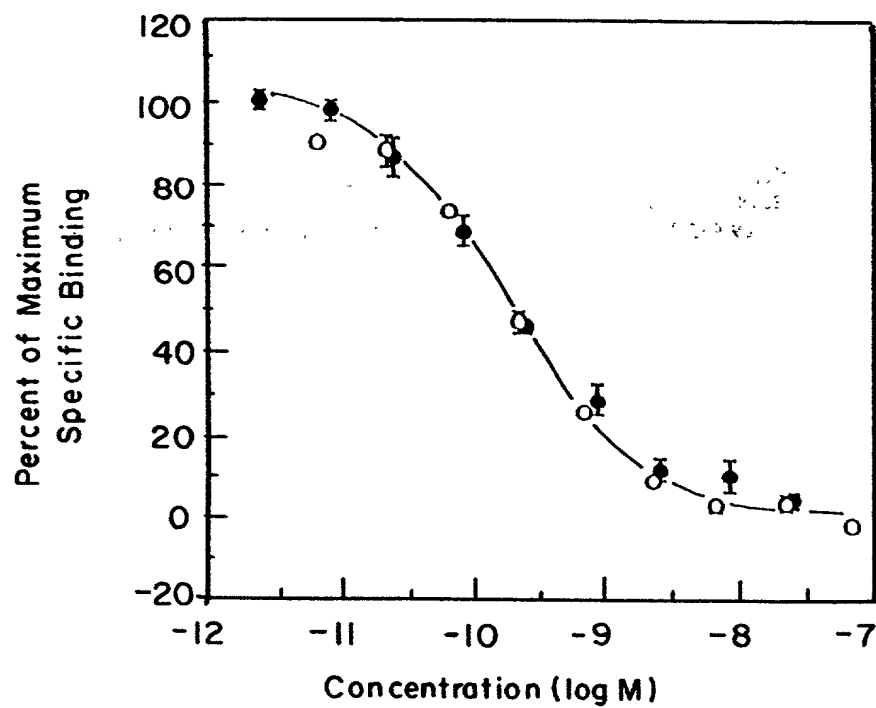


FIG. 29

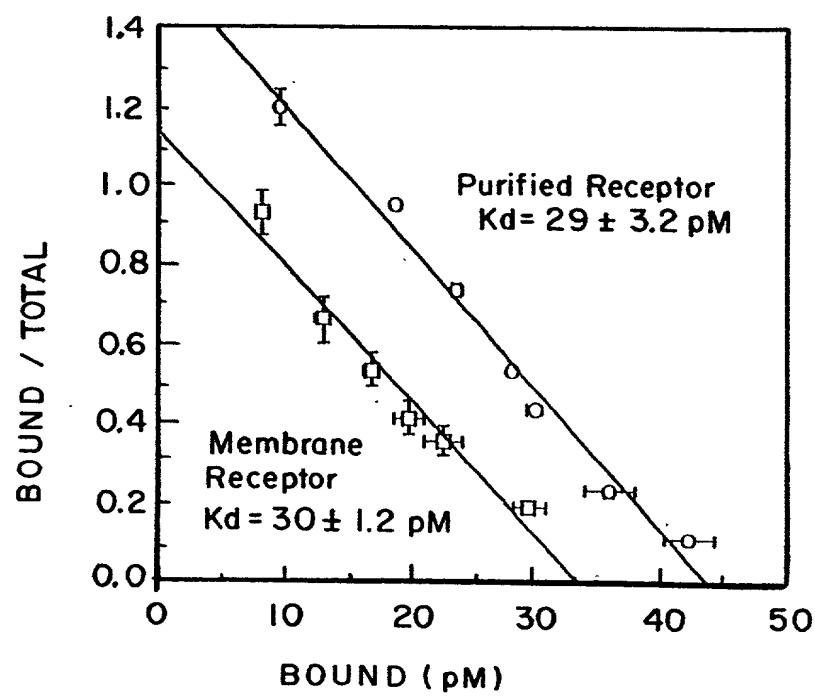


FIG. 30



FIG.31

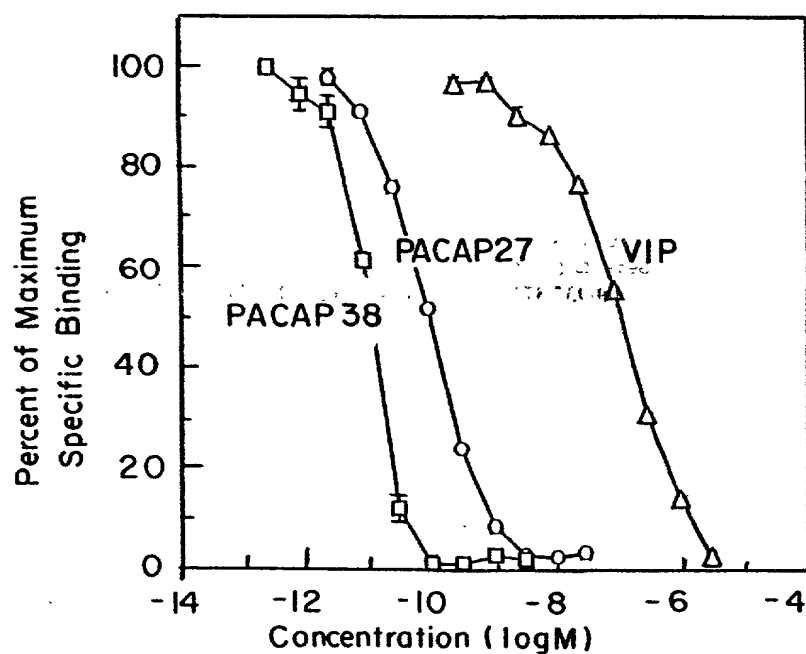


FIG.33

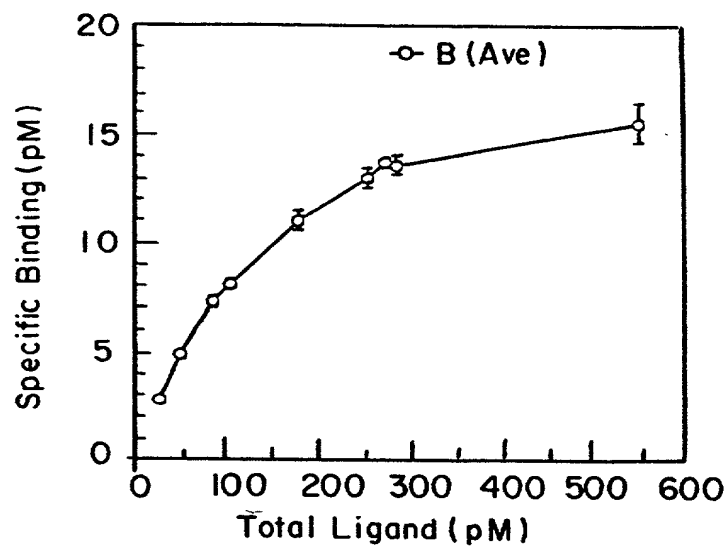


FIG.34

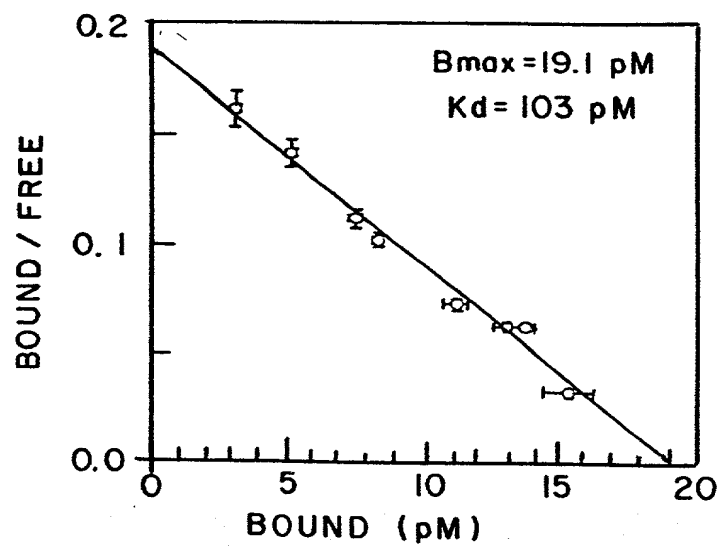


FIG. 35

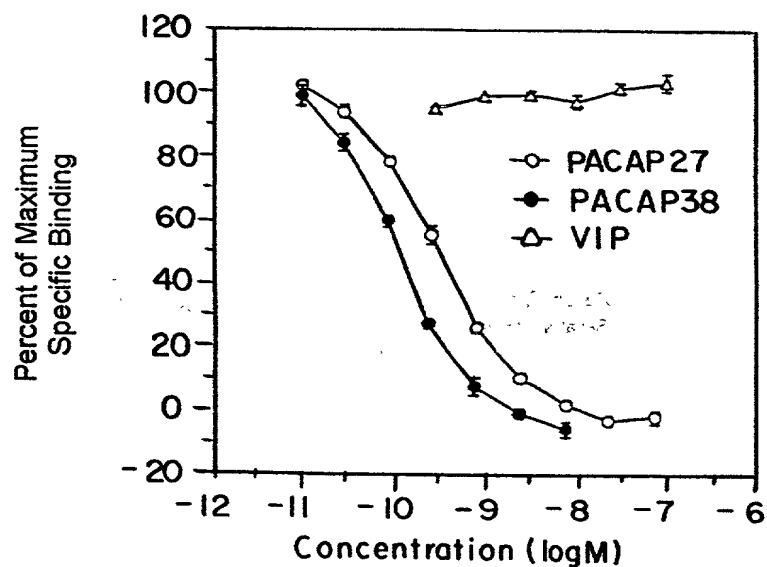


FIG.36

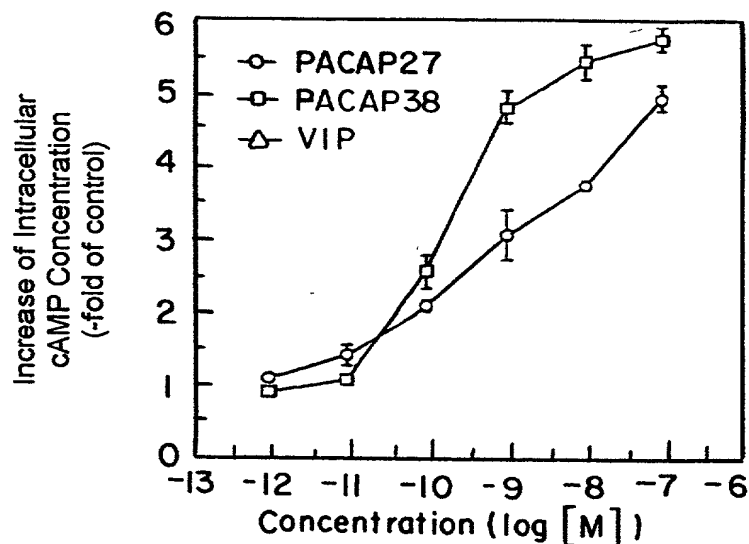


FIG.37

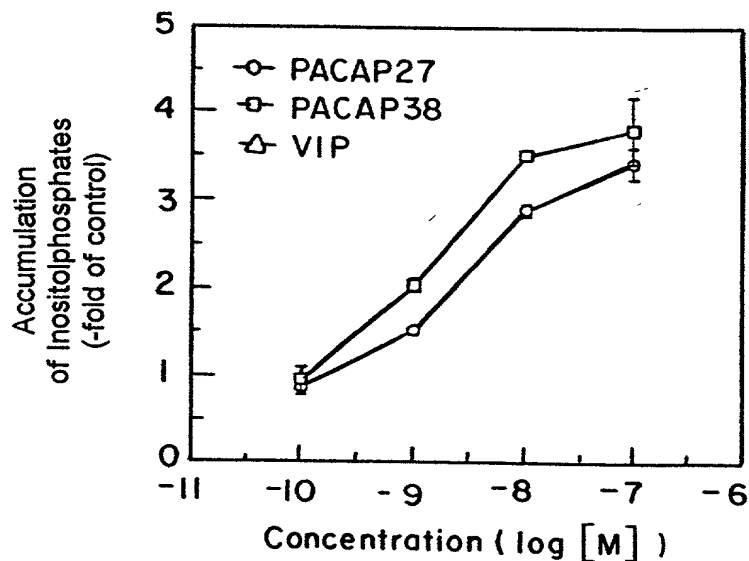


FIG.32

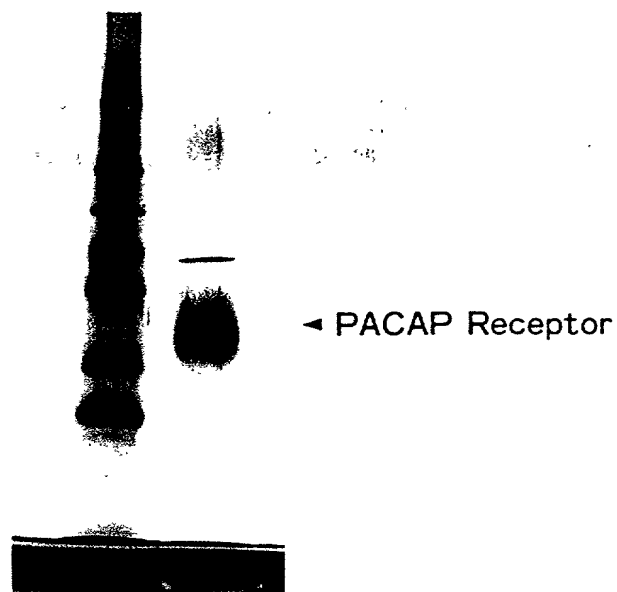


FIG.38

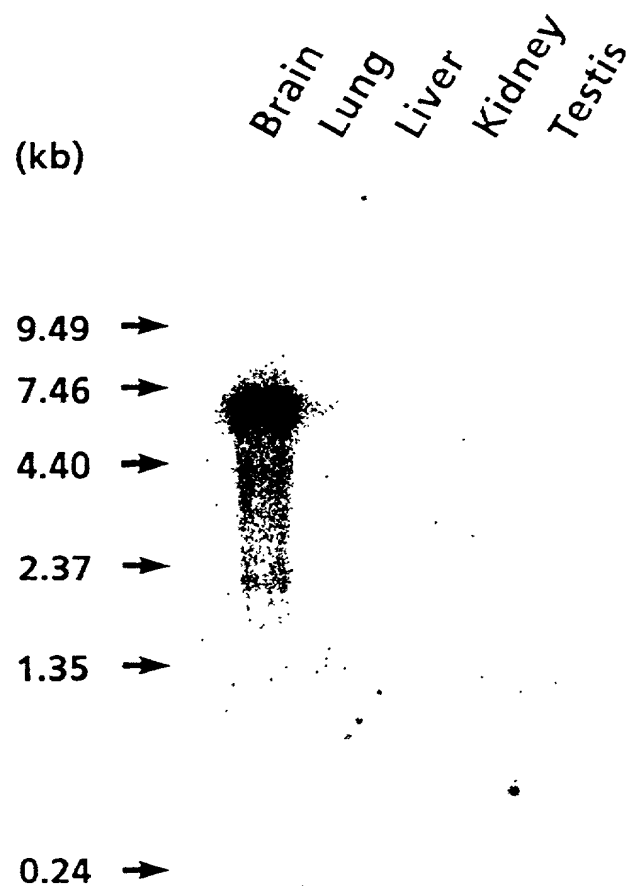


FIG.39

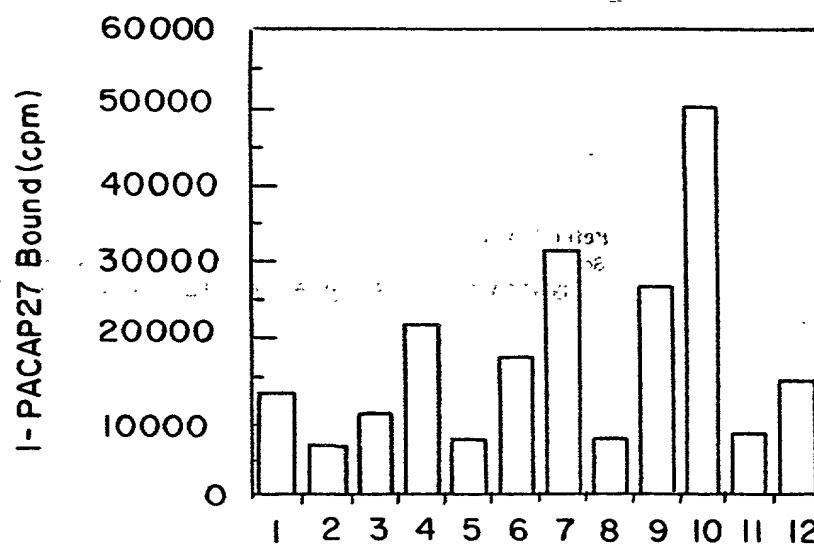


FIG.42

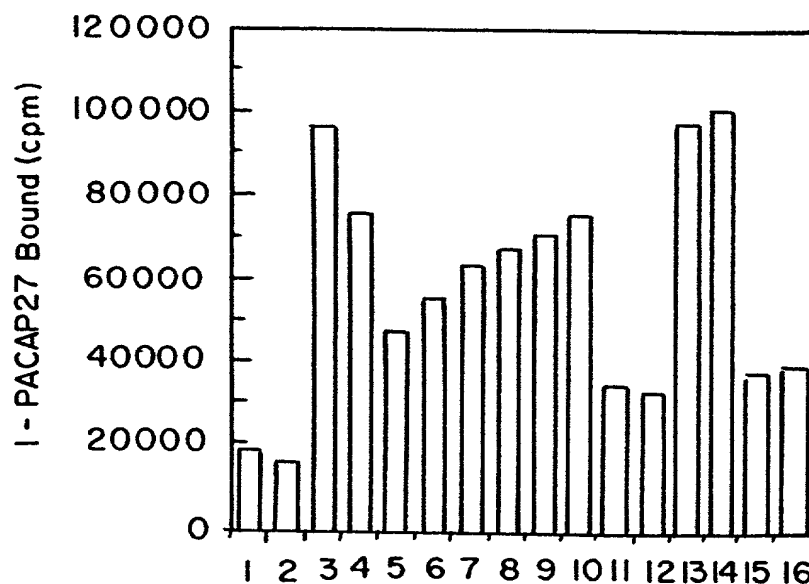
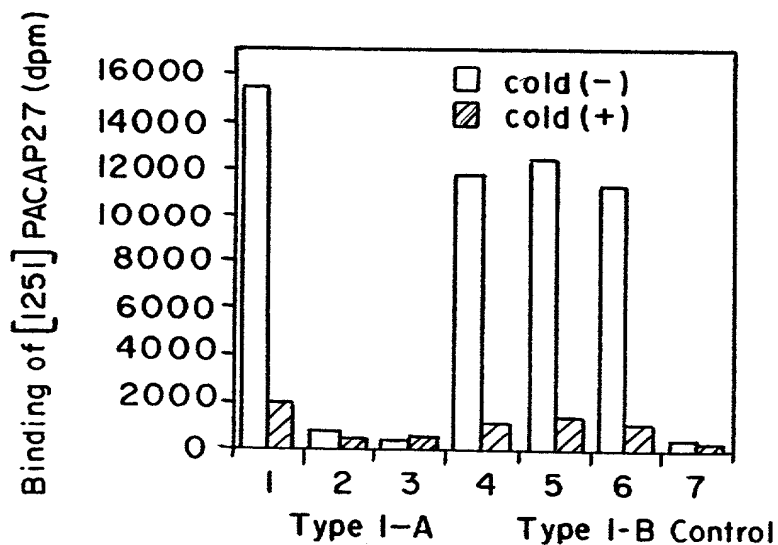


FIG.44



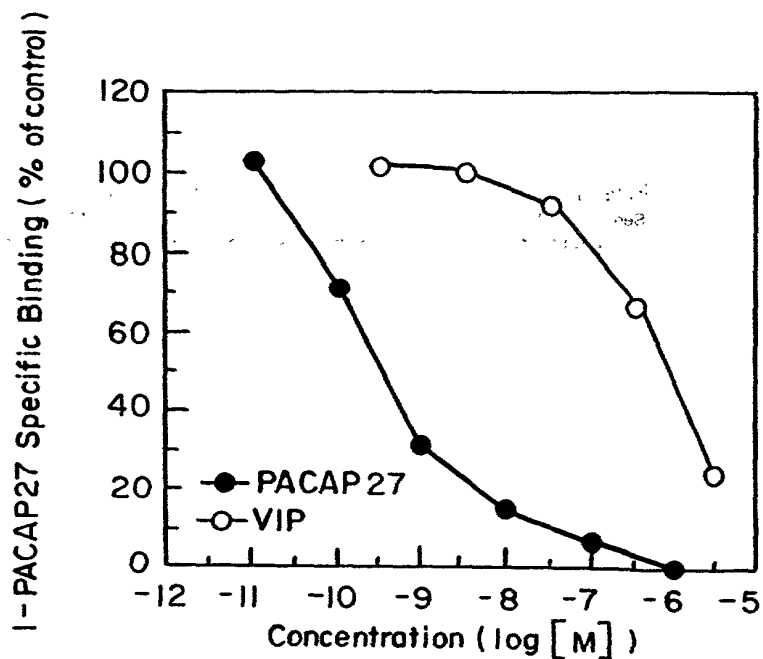


FIG. 40A

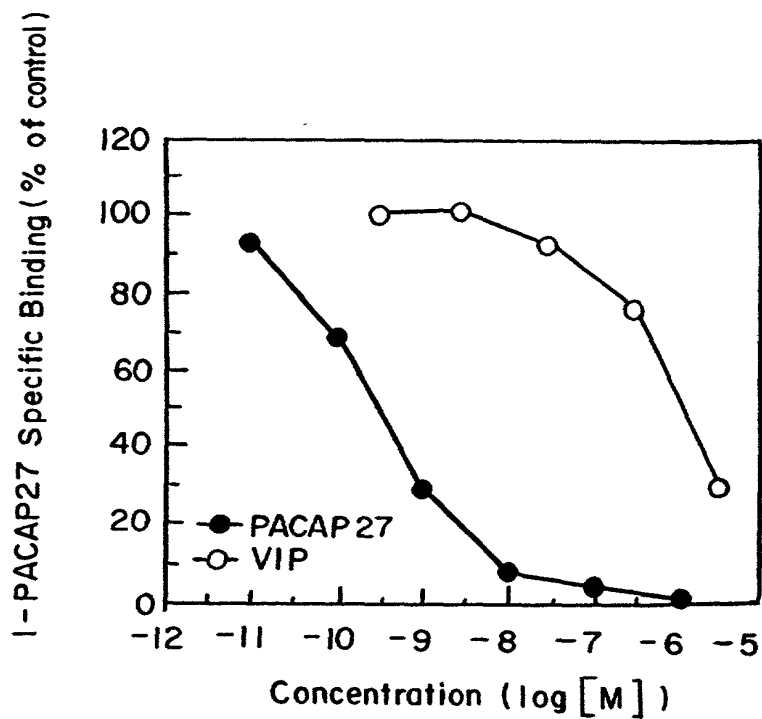


FIG. 40B

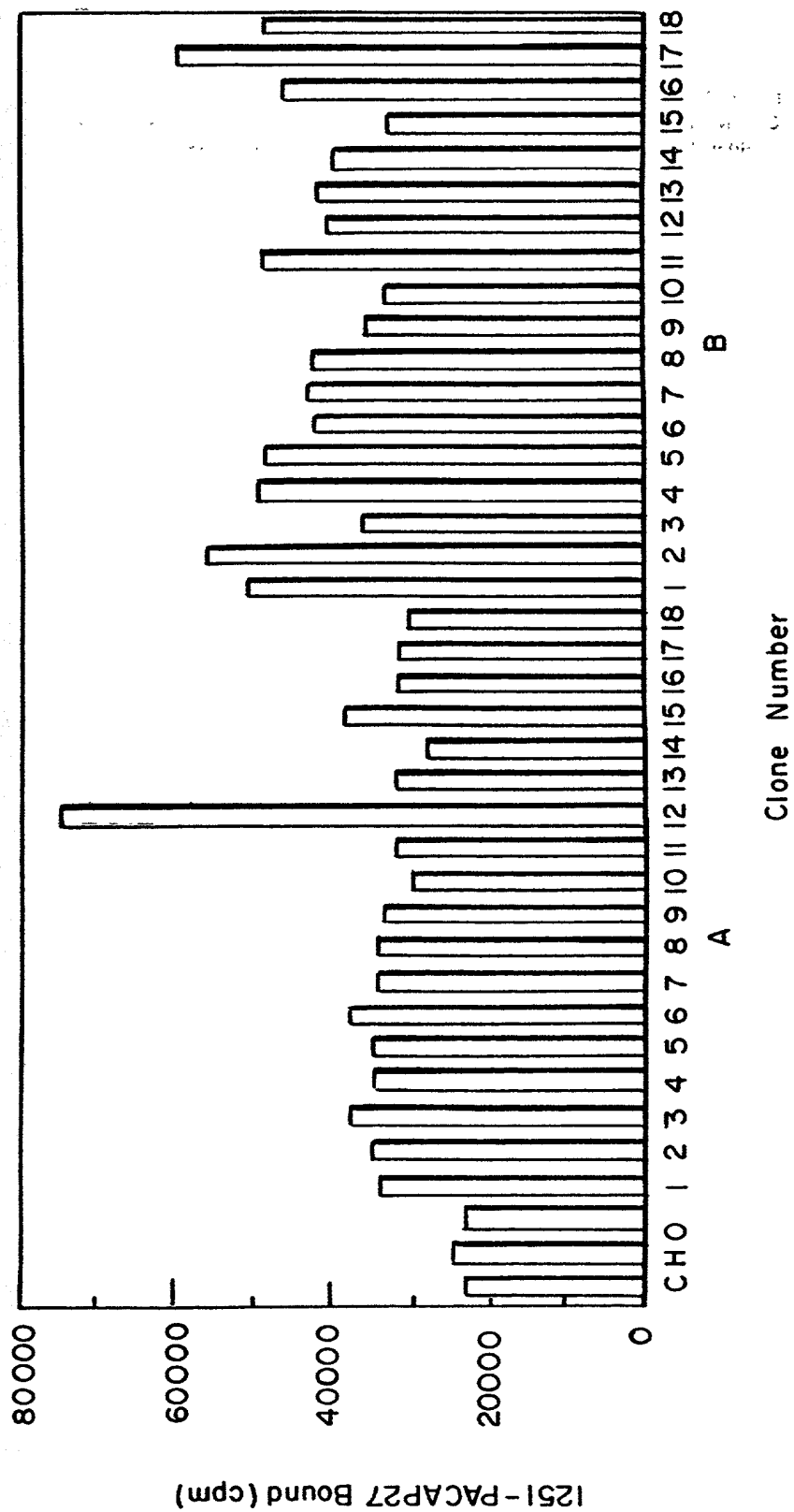


FIG. 41

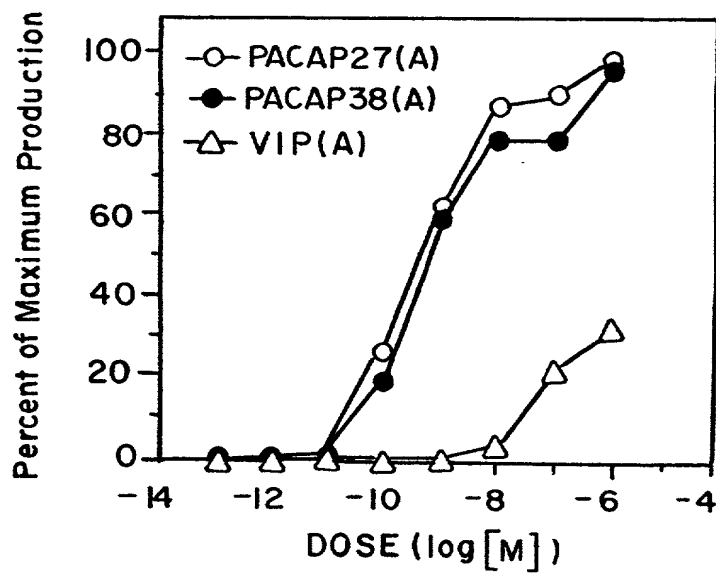


FIG. 43A

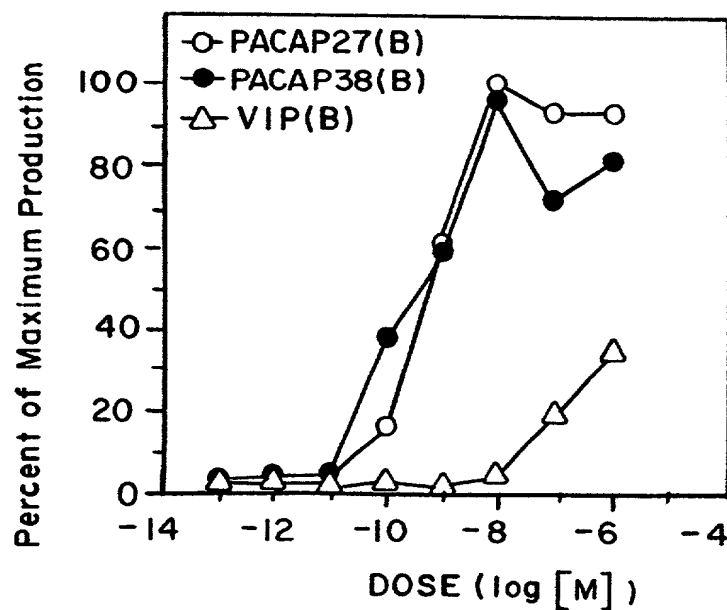


FIG. 43B

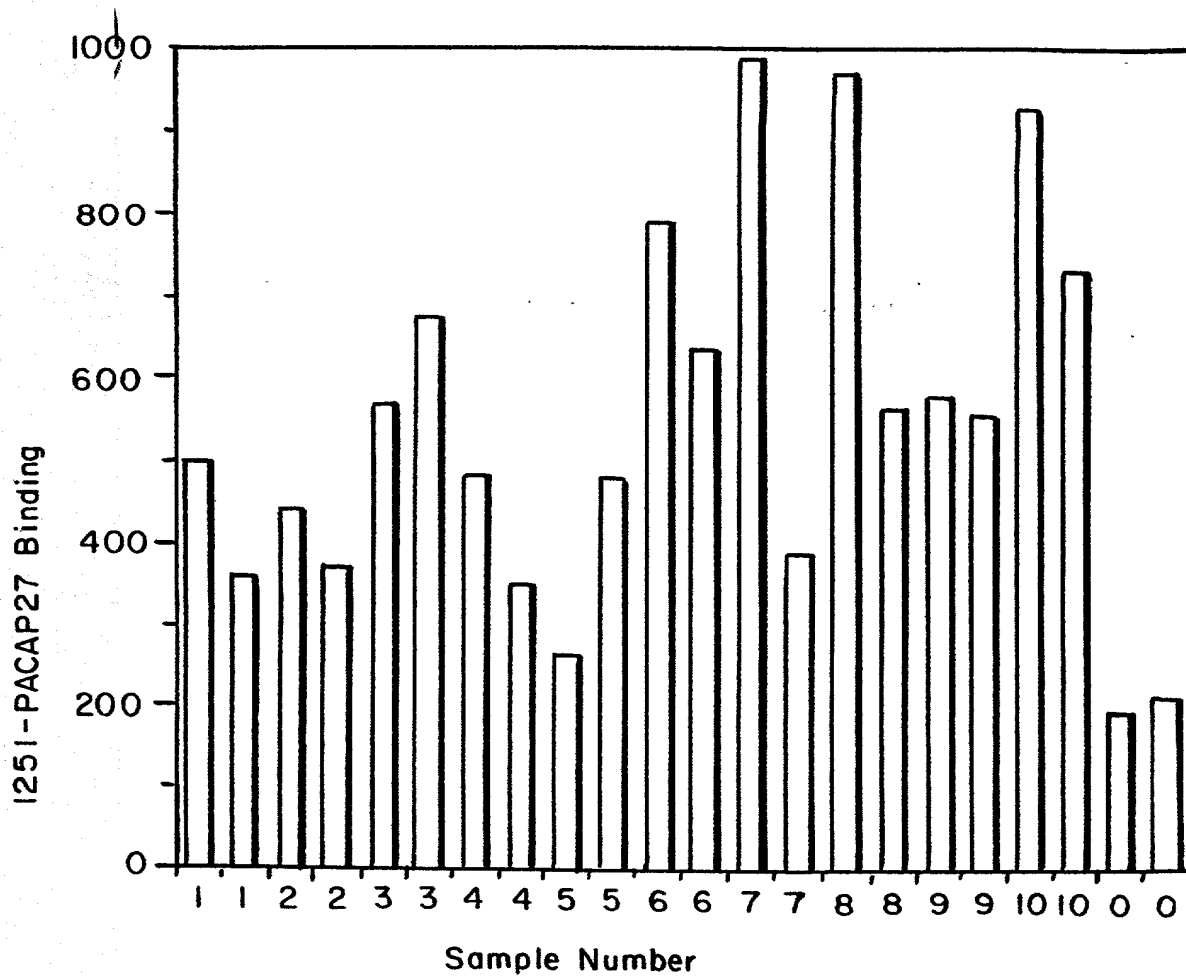


FIG. 45

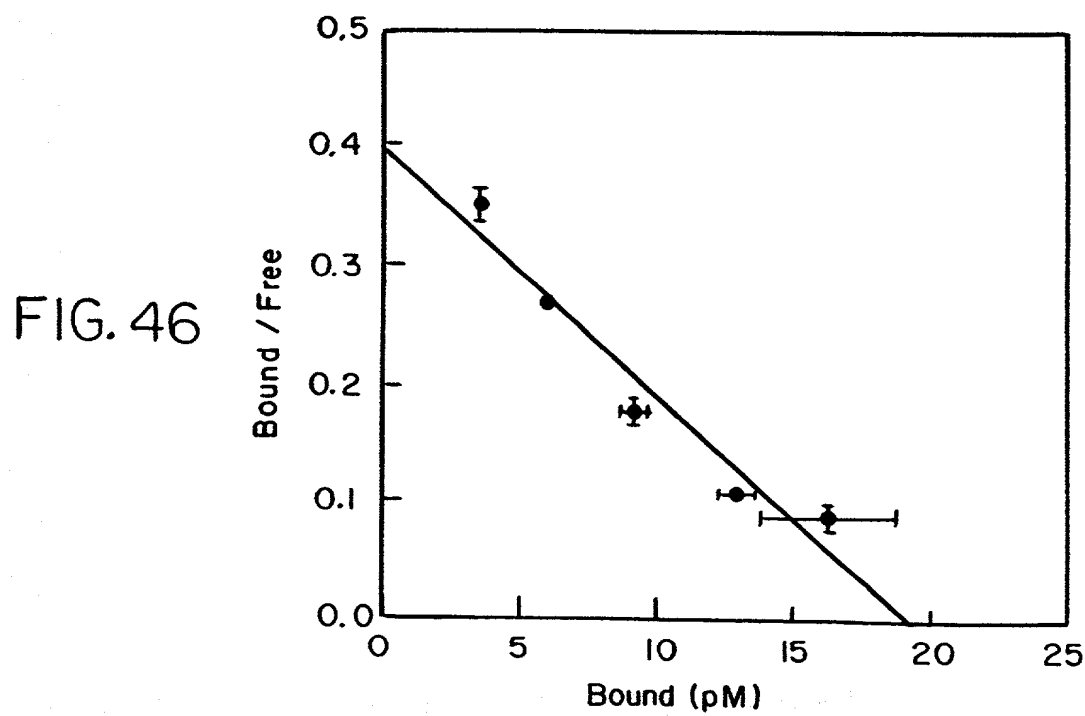




FIG.47

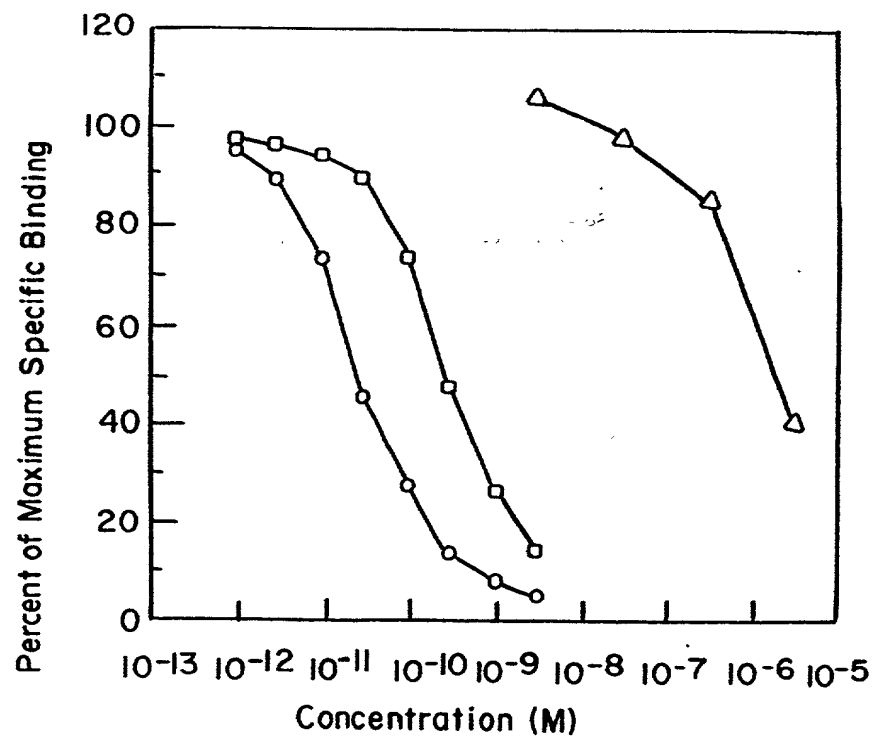
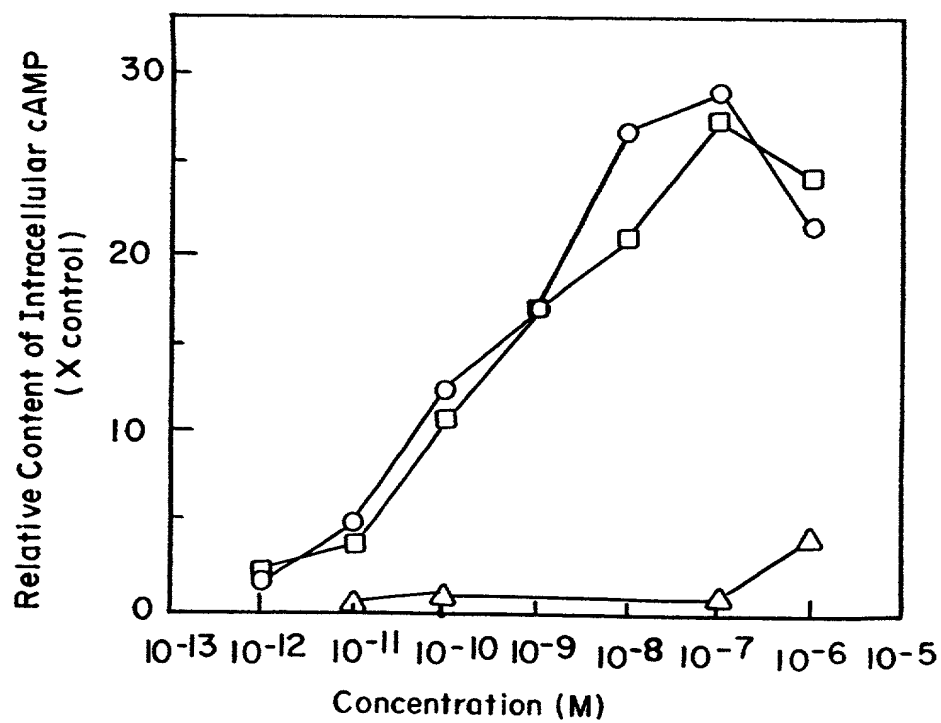


FIG.48



(kb)

Brain  
Lung  
Liver  
Thymus  
Spleen  
Pancreas  
Placenta

9.49 →  
7.46 →  
4.40 →  
2.37 →  
1.35 →  
0.24 →

(kb)

Olfactory Bulb  
Amygdala  
Basal Ganglia  
Hippocampus  
Thalamus  
Hypothalamus  
Cerebral Cortex  
Medulla  
Cerebellum  
Spinal Cord  
Pituitary

9.49 →  
7.46 →  
4.40 →  
2.37 →  
1.35 →  
0.24 →

FIG. 49

FIG. 49 shows the results of a Southern blot analysis of DNA from various tissues. The DNA was digested with EcoRI and probed with a cDNA probe. The results show that the probe hybridizes to a single band in all tissues, indicating that the gene is expressed in all tissues.

FIG. 50

FIG. 50 shows the results of a Northern blot analysis of RNA from various tissues. The RNA was probed with a cDNA probe. The results show that the probe hybridizes to a single band in all tissues, indicating that the gene is expressed in all tissues.

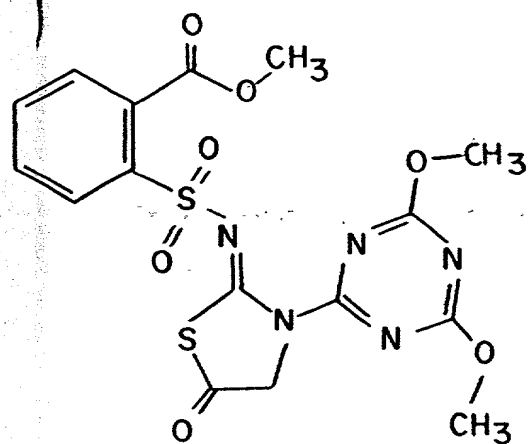


FIG. 5IA

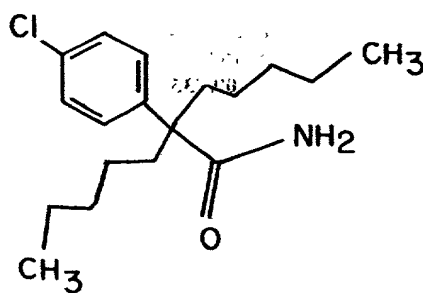


FIG. 5IB

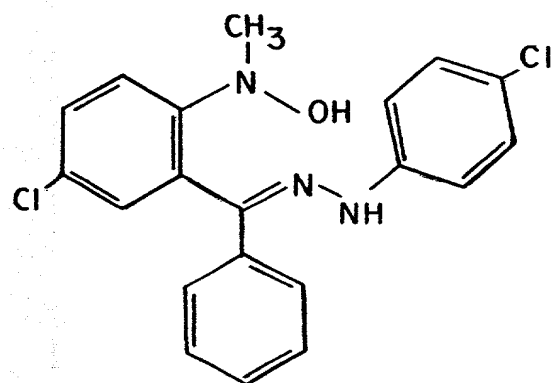


FIG. 5IC

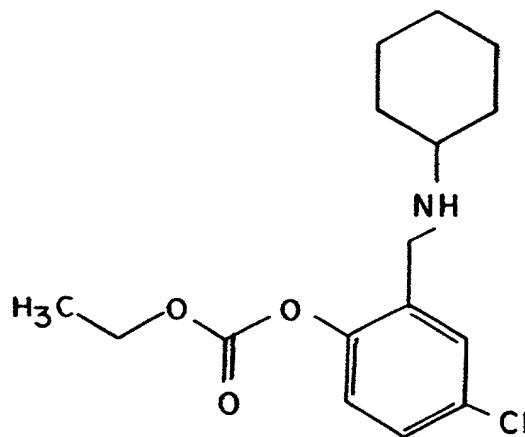


FIG. 5ID

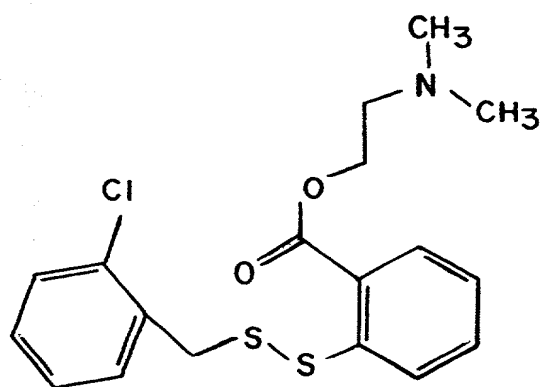


FIG. 5IE

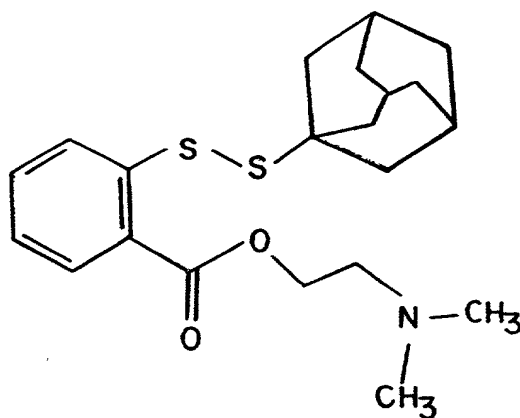


FIG. 5IF

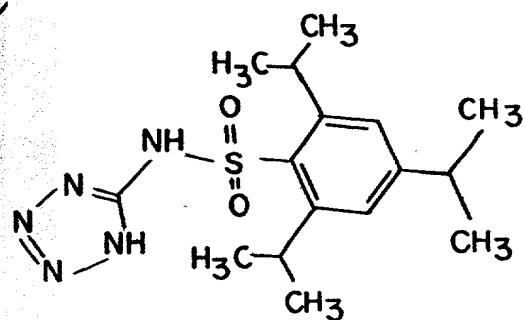


FIG. 5IG

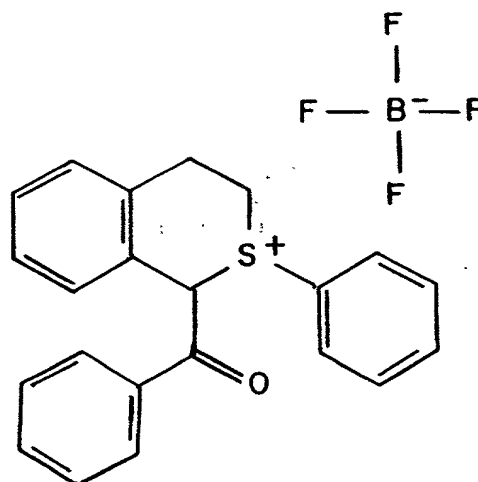


FIG. 5IH

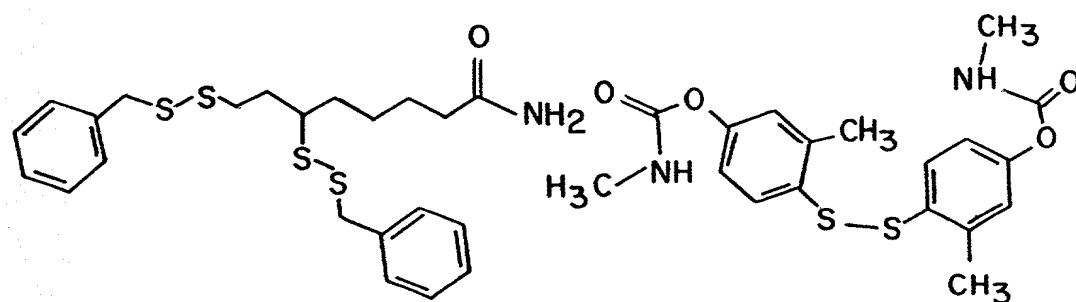


FIG. 5II

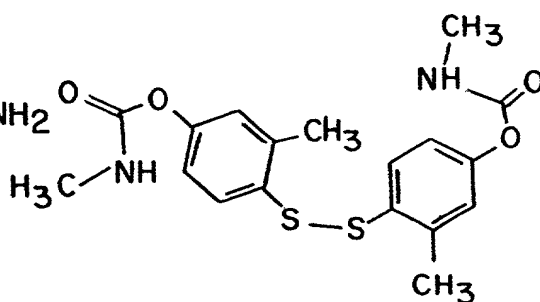


FIG. 5IJ

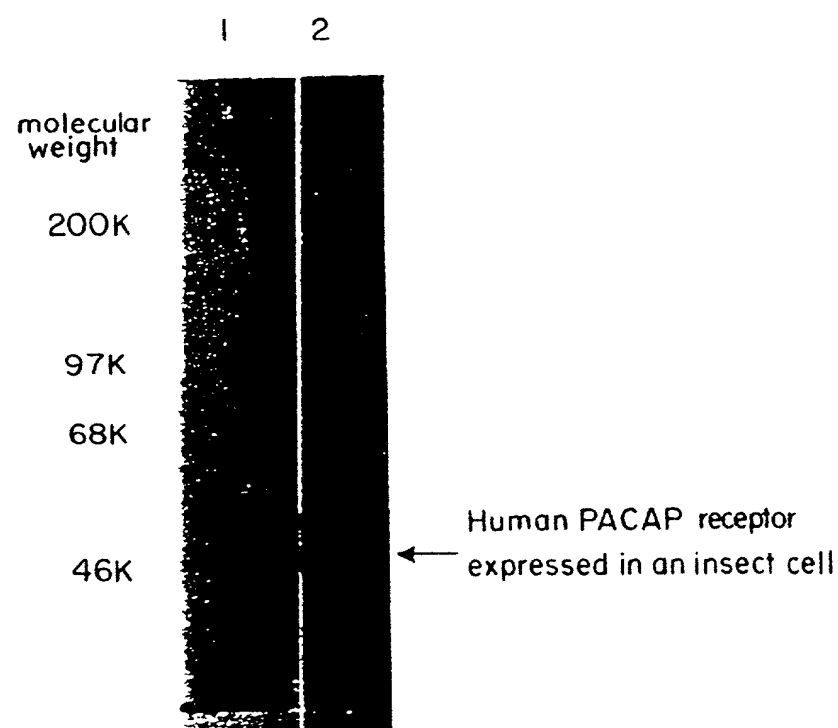


FIG. 53

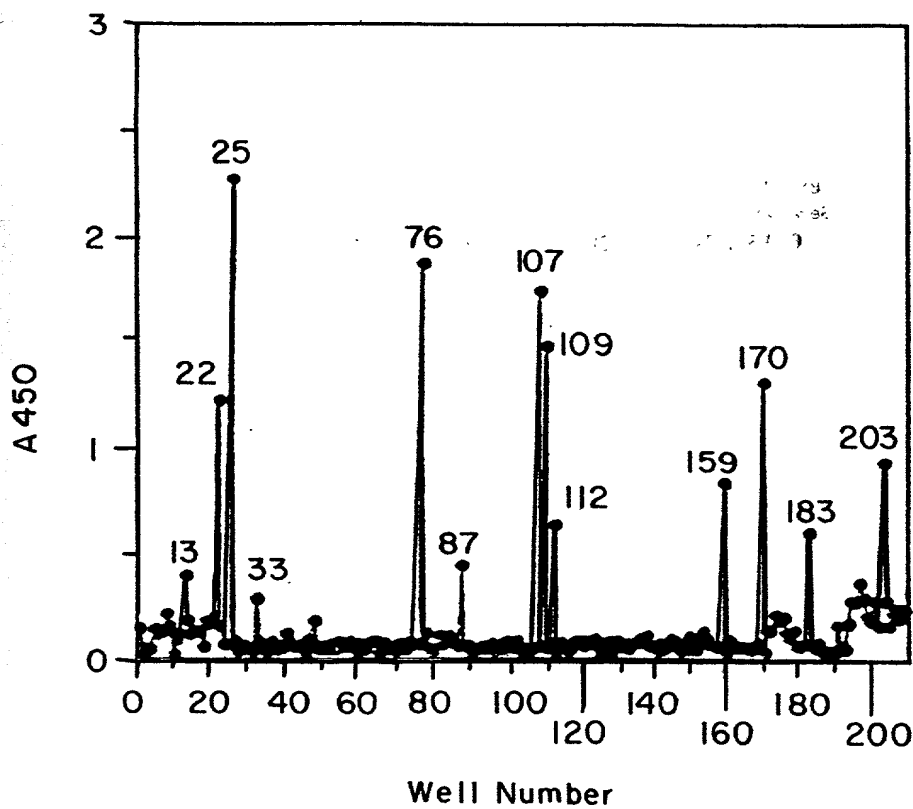


FIG. 52

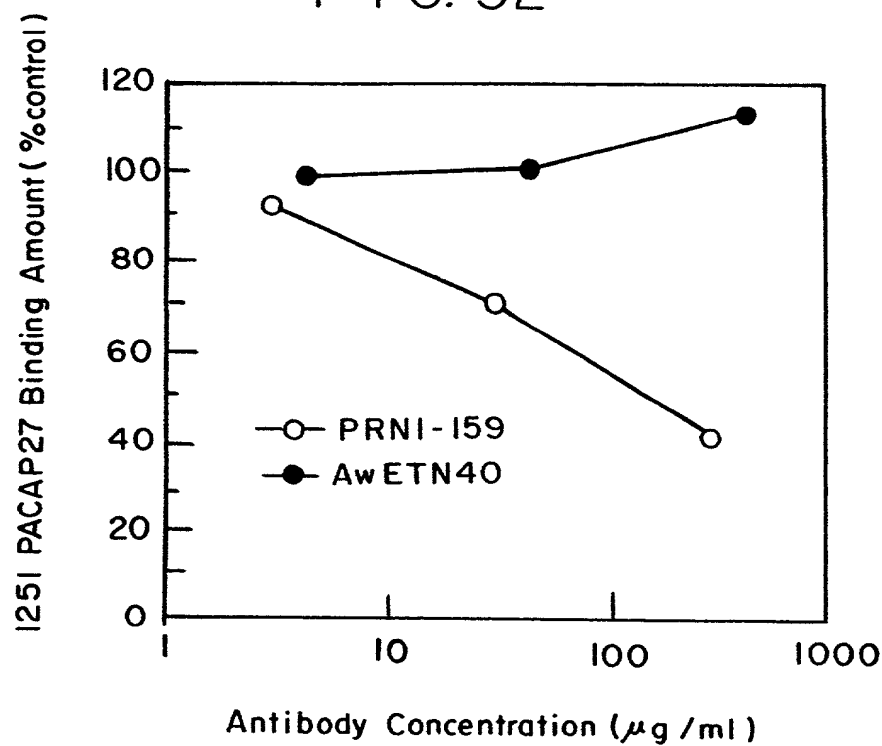


FIG. 54